PRINCIPLES AND PRACTICE
OF SURGERY

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By

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TO

HENRIETTA

MY WIFE

This book is

affectionately dedicated

PREFACE

Science may be defined as systematized knowledge. Since the practice of surgery defies exact formulation, it must remain an art, or a system of knowledge made efficient by mental and physical skill. Obviously, the more perfect the scientific part of surgery becomes, the more useful and beneficial will be the art of surgery.

The basic sciences then must be learned, reviewed, and applied to the clinical practice of medicine. This is doubly true in the application of surgical measures for the care and cure of disease processes. A knowledge of embryology enables the surgeon to understand congenital anomalies; anatomy is necessary in diagnosis and operative procedures; histology helps him understand pathological states; and etiology often teaches him how to avoid and correct them. Applied physiology is paramount in the practice of surgery. Such states as anoxia, shock, hemorrhage, endocrine imbalance, and subhydration are but a few of many examples that may be mentioned. A knowledge of biochemistry is necessary for the proper evaluation of such states as acidosis, alkalosis, tetany, and calcium imbalance and may point the way for a clearer concept of the formation of biliary and renal calculi. The sterols alone may open the door to the secrets of such diversified conditions as nerve and endocrine function, carcinoma, biliary calculi, and cardiac disease.

This book is written with the idea of correlating the basic sciences with the fundamental principles of surgery. Upon such a foundation can be erected the structure of clinical surgery—etiology, diagnosis, symptoms and signs, prognosis, and treatment, even to the minutest detail of technique.

The body of the book carries the "conquered ground" of surgical diseases; however, the correlated facts, the physiology, and even the unconquered experimental fields from which the ultimate truths will emerge have not been neglected. In both instances the discussion is relatively brief; however, if this book accomplishes that which the medical teacher tries to achieve, it will inspire the student to search through the selected references for more complete information.

The references quoted have been used extensively. Some of the data are given verbatim; most are interpreted by the author in the light of his own experience or in the experience of his advisors. It is his desire that full credit be accorded the many books, journals, and personal communications included herein.

If at times the text seems dogmatic, it is because the student must have a definite course charted for him so that he be spared the ordeal of drifting aimlessly among the waves of conflicting opinion. This is necessary until he may acquire surgical judgment—that intangible, essential attribute which gradually evolves through direct personal knowledge, procured by astute observation, actual practice, and constant persistent research.

The response to my first work, *Synopsis of the Principles of Surgery,* has encouraged me to produce this new book. Some information which appeared in the first book as "conquered ground" has been relinquished. Much that appeared in the footnotes as the "unconquered territory" of the experimenter has been won. Still more that was predicted, fortuitously perhaps, as the possible result of future investigation, has come true. These changes, flavored by the helpful and constructive criticisms of colleagues and reviewers, have been made in the pages that follow.

This new text deals chiefly with fundamental principles of surgery and is not intended as a monograph on every surgical specialty. However, surgical techniques are discussed. If a proper perspective is to be achieved, a good surgical specialist must first be a good general surgeon.

The writer of a text is presumed to have an intimate knowledge of the subjects he describes. This is the result of experience in most instances, but in many cases he must turn to other writers and observers for help. The references are designed to guide the student to proper authority in each particular field. The more highly specialized branches of surgery need special interpretation. To secure these I have turned to competent members of the respective groups for help and advice.

To my friends and advisors and to my loyal students, interns, and residents I give my sincere thanks. A few names of those who helped in the production of this book should be given special mention: Dr. Frank Forry, Dr. Clyde G. Culbertson, Dr. John L. Arbogast, and Dr. Amos C. Michael, of the Department of Pathology, have aided in procuring and properly interpreting pathological specimens; Dr. R. M. Harger gave splendid suggestions in the preparation of the chapter on acid-base balance; Dr. George J. Garceau gave good counsel on the chapter relating to orthopedics; and Dr. John A. Campbell selected and interpreted interesting x-ray films.

Dr. Edward J. Berman acted as my severest critic on the context and contents of the book, and in addition he aided materially my attempts to employ English that fulfills the requirements of proper syntax and semantics. Dr. Joseph F. Ferrara helped in the tiresome but important task of reading the proof.

Dr. Bertram S. Roth has provided valuable information concerning blood dyscrasias in infants and children. He has also answered many

questions relating to such vital functions as oxygen requirements, water *balance, and protein metabolism in infants.*

Since illustrations reveal more than words, Mr. J. F. Glore, medical artist, deserves special praise for the splendid drawings, diagrams, and photographs.

The typing of a book is a huge task in itself, but when in addition it requires a deciphering of the hieroglyphics of poor penmanship, it becomes a mountainous detour—such was the task of Mrs. Cecilia Suess, my meticulous stenographer, to whom I am grateful.

Mrs. Mildred Chandler, my faithful secretary, aided in reading the typewritten pages and relieved us of a mass of detail in the execution of this involved work.

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PART I

GENERAL CONSIDERATIONS OF SURGICAL PRINCIPLES

Chapter 1

HISTORICAL REVIEW

A book on the principles of surgery must not be limited to any one particular branch. It must contain the fundamentals of medicine as applied to surgical pathology and clinical surgery. It has been aptly said that the best textbook of surgery is a good textbook of medicine.

The historical approach to a subject enhances our understanding of it. If we wish to appreciate America, we must know some of the historical background of this country or our appreciation is limited. If we wish to approach a certain surgical subject, we must know, at least in a superficial way, what preceded present-day knowledge. As Osler put it, "The past is a good nurse, especially for the weanlings of the fold."

Much of the historical review will revolve about individuals. This is true because of the separation of men and distant places. Travel was limited, printing came later and even then great distances separated men. Today we speak of a trend which is broad and inclusive. The world is indeed one world as Wendell Willkie has put it. Men simply represent such movements as are occurring, whether they be in medicine, sociology, or government. They cannot, as individuals, initiate control, alter, or stop them. This is the reason for the lack of contemporary names in the present century.

Prehistoric man had some knowledge of surgery. He treated disease mostly by incantation and all sorts of superstitious practices; occasionally an archeologist uncovers a body of an early man that has a surgical trephine opening in the skull. Following the prehistoric period comes what Garrison calls the period of Egyptian and then Sumerian and Oriental medicine (4500-3000 B.C.). Much information concerning this time is obtained from Ebers' *Papyrus* (1500 B.C.). This document was discovered by George Ebers at Thebes in 1872. The code of Hammurabi (2250 B.C.) is also an important contribution. This includes Babylonian and Chinese practice and some Biblical laws. Although their knowledge was very primitive, some of their teachings are still good. They practiced quarantine. Their moral and ethical laws are still the standard of the civilized world. In this period they knew of leprosy but they did not know its etiology. If we read the book of Leviticus we find that a leper is unclean: he must be isolated and no one must enter his house until he is

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The deductive method of reasoning goes from the universal to the particular, from all to some, from the whole to its parts. It analyzes a premise and then proves it to be correct. This is known also as *a priori* logic, meaning the hypothesis that came before. The objection to this type of reasoning is that the major premises may be wrong, yet the logic sound, forcing the reasoner to a fallacious conclusion. Such reasoners are known today as sophists. (The original sophists were profound scholars.)

Induction is reasoning from the observed parts to a whole, from particulars to generals. It synthesizes the results of experimentation and discovery. This is also known as *a posteriori* logic. We must observe carefully and, if necessary, experiment in the laboratory, then synthesize our findings, and finally from all known facts we come logically to the correct conclusion.

Byzantine Period (A.D. 476-732). "A period known for its extreme luxury, licentiousness, profligacy and lack of accomplishment." "Byzantium is now known as Istanbul. With the downfall of the Roman Empire, Eastern scholars began to pour into Europe. **Paul of Aegina** (A.D. 625-690) stands out during this period. He was a surgeon. He knew of lithotomy, trephining, tonsillectomy, paracentesis, mastectomy, eye surgery, and military surgery. He knew how to pull teeth; he is said to have insisted that a dental forceps be made of soft lead. Did he think there could not be much wrong with a tooth if it took strong iron forceps to extract it? Or conversely, did he believe that if the tooth were dead and infected it would act as a foreign body and become loose so that its removal could be accomplished easily?

The Dark Ages (A.D. 476-1000).

This was the *Age of Feudalism* (from *feodum* or *feudum*, a fee or fief) which came into existence because individualism afforded no protection to life or property and because decadent monarchies were too loosely organized to give such protection. Consequently, the feudal lords came into power and the strongest and most powerful individuals took over the land and became the local rulers. The rest of the populace became vassals and serfs who banded together and worked under the lord in return for his protection. Feudal states were formed and feudalism remained until the medieval period, when kings arose from their previous lethargy, took back some of their territory, and gave royal titles to the feudal lords. All medical papers were written in Latin so that secular knowledge would not undermine the ecclesiasticism which prevailed. Men kept their "knowledge" to themselves. There was an air of mystery around the physician. The church helped during these Dark Ages. The monks did some experimental work in their monasteries which did not come to light until later.

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well. Then the priest will order the destruction of that house. They knew of certain surgical operations, although the Bible seldom speaks of any except circumcision.

Ritualistic circumcision was usually done on the eighth day of life and this custom is still retained. The reason for this practice was probably based on the observation that hemorrhage was more likely to occur if the operation were done earlier. It is now known that at birth and for about six hours thereafter the prothrombin level is normal. Apparently the reserve of this substance is limited and at twenty-four hours reaches a low level. This is due to a lack of vitamin K, which is not synthesized in the intestine until the infant begins to take food. Although bacteria are found in the colon within eight hours after birth, they probably are not present in sufficient numbers to produce this essential vitamin.

Greek medicine played a very important role in medical development. *Aesculapius,* who lived about 3000 B.C., is called the god of medicine. The Greeks thought he was a living personality. He is now thought to be a mythical figure, the son of Apollo and Coronis. He was trained by Centaur, who was half man and half horse. He antagonized Zeus, the god of gods, who slew him. He had two daughters, Hygeia and Panacea. Hygeia (prevention of disease) was known as the goddess of health; Panacea (derived from the Greek work "all-healing") is today used to describe a cure-all in medicine or treatment.

Hippocrates (460-370 B.C.) is held to be the father of medicine. He was a real character. Every student of medicine should read the notes and comments of Hippocrates and his sayings. He taught by aphorisms or maxims.

An aphorism is a concise statement of principle; a maxim, of medical art.

This is an excellent pedagogical method and will be used wherever possible in this book. It is difficult because many parts of medicine do not lend themselves to such synthesis. Hippocrates knew the many viscissitudes of medicine when he said: "Life is short, and the Art long; the occasion fleeting; experience fallacious, and judgment difficult."

Celsus lived during the reign of Tiberius Caesar. He was probably not a physician, but he wrote extensively on medical subjects. His *De Re Medicina* was one of the first books printed in the Renaissance (1478). It consisted of eight books; the fourth contains the four classical signs of inflammation (Chapter 10). The seventh contains the first account of the use of the ligature.

Galen (A.D. 131-201) (Greek physician in Rome) was a great man. He was so great that for a thousand years after his death medical men still preached and taught some of his correct as well as erroneous views. Many of his teachings were right. For example, he knew that the arteries contain blood and not air as was previously taught. He described inflammation and distinguished between arterial and venous blood. He thought, however, that blood passed from one side of the heart to the other by seep-

ing or "sweating" through. He was a great deductive thinker. He would sit at a desk and put down a statement and work from there to a logical conclusion, but he also used inductive methods.

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(although with a different meaning) in the light of modern studies. Medical men looked down upon surgery with disdain and they looked upon the barber-surgeon as a craftsman, which indeed he was.

The barber-surgeon did two things; blood letting and "cutting" for stone. The modern barber still displays the red and white striped pole (symbolic of an extremity with blood flowing in spiral fashion).

Today surgery has come to be the *chief form of medical treatment*. In this respect, it is very much as the science of bacteriology was before it developed to its present degree. Books on botany and biology formerly had only one paragraph on bacteria. So it was with surgery in relation to medicine. *Today surgical knowledge has accumulated so fast that it equals* its parent subject. But it still must be studied in its proper relationship. The surgeon must be a good medical man first and then a surgeon in addition. He has two responsibilities instead of one.

The Renaissance or the Revival of Learning (1453-1600).

Outstanding events of this period were the fall of feudalism, migration of Greek scholars to Europe, the invention of crude methods of printing, and the discovery of America in 1492. The Chinese knew of printing many years before, but it was not available to Europeans. Other epoch-making accomplishments during this age were the introduction of gunpowder, the discovery of the southeast passage by Vasco da Gama, Magellan's circumnavigation of the globe, heliocentric astronomy by Copernicus, the migration of Byzantine scholars to Europe after the fall of Constantinople in 1453, and the separation of church and state.

There were many great man in medicine during this period. We can mention only some of the more outstanding. Paracelsus (1493-1541) (*whose real name was Aureolus Theophrastus Bombastus von Hohenheim*) lived in Switzerland most of his life and was far in advance of his time, discarding Galenism and the Four Humors (blood, phlegm, yellow bile, and black bile). He advocated cleanliness in surgery and fought for the unity of medicine and surgery. He taught one principle that we teach *today—it is the guiding philosophy of surgical treatment*—". . . by their nature the tissues contain an inborn balsam that heals wounds. So should every surgeon know that it is not he, but nature that heals wounds."

In his day surgeons *cauterized wounds with hot irons, thereby retarding* healing. It has only been a short time since it was deemed necessary to change all surgical dressings daily. *Now a surgical wound is unmolested* for seven to ten days after a "clean" operation unless there is pain, fever, or inordinate drainage. Observe an injured dog. He lies with the injury exposed to the air and sun and keeps it moist by frequent licking. Such wounds are rarely infected, having healthy granulations, and heal with small amounts of scar tissue.

We are just coming through the *age of antiseptics*. It was once thought that the stronger antiseptics were best. Then different-colored dyes were employed. An attempt will be made to show in this book that antiseptics have a place but are not as *important* as was formerly thought. The emphasis today is on providing conditions which will help the body and its cells (nature) to annihilate the invading organisms, and it is now believed that in most instances some inert, soothing substance such as

physiological saline is preferable. *For any antiseptic that is strong enough to kill bacteria is strong enough to kill cells, and healthy cells are more important than temporary sterilization.*

Leonardo da Vinci (1452-1519), the artist who painted the Mona Lisa, drew excellent anatomic charts.

Andreas Vesalius (1514-1564) was one of the pioneer anatomists. He was one of the first to take the time to dissect the human body. This he had to do in his own room and then it had to be done so surreptitiously that no one would discover it.

Ambrose Paré (1510-1590) popularized anatomy by writing in the vernacular. He is the man who reintroduced the ligature for the control of hemorrhage. The story is told that at the Battle of Metz one of the soldiers had his arm shot off. It was the custom at camp to use boiling oil or hot irons for cauterization (comparable to strong antiseptics today) but neither was available. To arrest the hemorrhage, Paré tied the bleeding vessels and nothing more. The man recovered. The second great maxim in surgery which in one sense corresponds with that of Paracelsus is one by Paré: *"Je le pansay; Dieu le gaurit"*—"I dressed his wounds; God cured him." The new surgeon just out of school does not believe this; but as his experience accumulates and wisdom supplants incomplete knowledge, he will not only admit its truth but will scientifically interpret it (see Chapters 3 and 10).

Girolamo Fracastorius (1484-1553) wrote a poem about a shepherd who had blasphemed the Lord and contracted the "big pox." He named the shepherd Syphilis, from Ovid's story of the son of Mobe. Mobe's second son was named Sipylus.

The Seventeenth Century has been called the age of individual scientific endeavor.

This is the age of Shakespeare, Milton, Cervantes, Velasquez, Rembrandt; the composers and musicians, Bach of Germany and Purcell of England; Molière, the dramatist, and Descartes, the philosopher and physiologist, of France, Leibnitz, Newton, Sir Thomas Moore; Sir Walter Raleigh; Bacon, Locke, and Spinoza; the Thirty Years' War; The Spanish Armada; and the Great Rebellion of 1643.

William Harvey (1578-1657), the great comparative anatomist, described the circulation of the blood in his paper "De motu Cordis." Before the time of William Harvey this was not definitely known. Harvey knew how the blood got down the arteries and back through the veins, but he did not know how it crossed from the former to the latter.

Athanasius Kirchner (1602-1680) and *Anthony van Leeuwenhoek* (1632-1723) discovered the microscope. The former described protozoa (contagium vivum); the latter saw the capillaries. This was a forward step toward the understanding of the circulation and proved that William Harvey was correct in his beliefs.

R. Lower is credited with the first transfusion of alien blood (1665). A. Coga also recorded this procedure in 1667. Transfusion is mentioned in Pepys' diary (Nov. 14, 1666).

John Hunter (1728-1793) lived in the *Eighteenth Cenury.*

In the eighteenth century such names as Kant, Rousseau, Voltaire and Hume and Pope stand out in literature; in music, Mozart, Haydn and Gluck, and Handel; in chemistry and physics, Lagrange, Laplace, Cavendish, Priestly, Lavoisier, Galvani, Volta, Franklin, Fahrenheit; in medicine, Edward Jenner (1708-1777), great physiologist. In America it is the age of Fulton and Stephenson and of the Declaration of Independence by our illustrious statesmen.

Had we visited London before World War II we could have seen in the museum of the Royal College of Surgeons a complete collection of most of his specimens. He died a poor man. His living room, bathroom, and yard were full of animals. He did not publish one-half of what he accomplished. Among many other experiments he ligatured the external carotid artery on one side of a deer. The antler did not become necrotic and break off. He reasoned that blood must be getting to it in spite of the ligature. By this experiment he discovered what we know today as collateral circulation, a phenomenon which usually makes it possible for the surgeon to tie an artery without causing gangrene. (See Chapter 17.) He described a method for curing aneurysms and one for repair of tendons. He inoculated himself with gonorrhea pus and then delayed treatment to study the disease. A chancre developed. Unfortunately, the patient from whom the pus was obtained had both gonorrhea and syphilis. Consequently Hunter confused the two. He also described shock, phlebitis, pyemia, intussusception, inflammation, and the care of gunshot wounds; in addition, he delved into the field of dentistry, naming the teeth and using human teeth for artificial dentures. He is undoubtedly one of the greatest comparative anatomists and surgeons that ever lived.

In the *Nineteenth Century Rudolph Virchow* (1821-1902), a great pathologist, taught that "all cells come from other cells *(omnis cellula e cellula).* Prior to his time men spoke of spontaneous generation. Our entire body is simply a mass of cells and they all come from one cell, the ovum. The fertilization and development of this cell give rise to all other cells in the body. Later they developed into organs and tissues, such as liver, kidney, skin, etc., which have separate characteristics and functions, but if we know cells, we know the unit from which the entire human being is constructed. That is why it is necessary for us to study histology and cellular pathology. *The reaction of the body as a whole depends upon the changes which may occur in the cell.*

Louis Pasteur (1822-1895), the diminutive French chemist, indirectly did more to make modern surgery possible than any one man. He discovered that living organisms cause putrefaction and proved the theory of "spontaneous generation" to be a myth. He made a very important statement that to us seems obvious—he said in effect that the germ had a

parent from which it came. His biography should be read by everyone in medicine. He was not a physician, but his careful analytical mind led him into paths that transformed the concept of medical practice. Besides determining that "sour" or spoiled wine was due to living organisms, he showed how heat and then cooling would kill these bacteria (pasteurization). He also introduced vaccine for anthrax and the method of immunization for rabies which is in use today.

Robert Koch (1843-1895) is regarded as the father of modern bacteriology. Pasteur evolved the theory and Koch discovered bacteria and practically developed the science of bacteriology. Prior to his time no methods of staining were available by which bacteria could be easily identified. He also taught us how to grow bacteria on solid media. His description and identification of the tubercle bacillus was epoch-making.

His five postulates proving that a given organism was the cause of a given disease were: (1) The microorganism must be present and demonstrable in every case of the disease; (2) it must be isolated in a pure culture; (3) inoculation from such culture must reproduce the disease in susceptible animals; (4) it must be reobtained from the animals; (5) and it must be grown again in a pure culture.

Koch thought that a vaccine could be made which would immunize an individual against the germ in every instance. He is reported to have said that an individual is more or less the victim of any bacteria he might encounter. Needless to say, in these latter concepts he erred, as Ehrlich and Metchnikoff subsequently showed by their studies in immunity.

A contemporary of Pasteur's and Koch's was the Englishman, *Joseph Lister* (1827-1912). *Compound fractures were almost 90 per cent fatal* in his time; today the mortality is extremely low. By using carbolic acid as an antiseptic he cut down the mortality in England from 95 to 40 per cent. He correctly predicted that the time would come when the mortality from compound fractures would be almost nil.

Nurses in that day would spray carbolic acid over the patient, the surgeon, and the room. Instruments were soaked in it. That was antiseptic surgery. Often a member of the staff or the surgeon would be overcome from carbolic acid poisoning during the course of the operation. Here we have an example of the slow and halting but persistent progress of medicine. First, as a result of Pasteur's and Koch's discoveries, bacteria were found to be the cause of suppuration in wounds; then Lister decided that he must kill these bacteria in order to get healing with a minimum of infection; then Halsted and others reasoned that it would be far better to exclude them as much as posible and thus today we have substituted so-called aseptic for antiseptic surgery.

Strictly speaking, modern surgery is not aseptic. Even after the most meticulous scrubbing and use of antiseptics the skin still harbors bacteria in the sebaceous glands and hair follicles. Only the "transient" bacteria have been removed. Furthermore, there are more bacteria in a surgical wound toward the end of an operation. These enter from the air and from the nose and the throat of the surgeons and nurses in

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John Hunter (1728-1793) lived in the *Eighteenth Cenury.*

In the eighteenth century such names as Kant, Rousseau, Voltaire and Hume and Pope stand out in literature; in music, Mozart, Haydn and Gluck, and Handel; in chemistry and physics, Lagrange, Laplace, Cavendish, Priestly, Lavoisier, Galvani, Volta, Franklin, Fahrenheit; in medicine, Edward Jenner (1708-1777), great physiologist. In America it is the age of Fulton and Stephenson and of the Declaration of Independence by our illustrious statesmen.

Had we visited London before World War II we could have seen in the museum of the Royal College of Surgeons a complete collection of most of his specimens. He died a poor man. His living room, bathroom, and yard were full of animals. He did not publish one-half of what he accomplished. *Among many other experiments he ligatured the external* carotid artery on one side of a deer. The antler did not become necrotic and break off. He reasoned that blood must be getting to it in spite of the ligature. By this experiment he discovered what we know today as collateral circulation, a phenomenon which usually makes it possible for the surgeon to tie an artery without causing gangrene. (See Chapter 17.) He described a method for curing aneurysms and one for repair of tendons. He inoculated himself with gonorrhea pus and then delayed treatment to study the disease. A chancre developed. Unfortunately, the patient from whom the pus was obtained had both gonorrhea and syphilis. Consequently Hunter confused the two. He also described shock, phlebitis, pyemia, intussusception, inflammation, and the care of gunshot wounds; in addition, he delved into the field of dentistry, naming the *teeth and using human teeth for artificial dentures. He is undoubtedly* one of the greatest comparative anatomists and surgeons that ever lived.

In the *Nineteenth Century Rudolph Virchow (1821-1902)*, a great pathologist, taught that "all cells come from other cells *(omnis cellula e cellula)*. Prior to his time men spoke of spontaneous generation. Our *entire body is simply a mass of cells and they all* come from one cell, the ovum. The fertilization and development of this cell give rise to all other cells in the body. Later they developed into organs and tissues, such as liver, kidney, skin, etc., which have separate characteristics *and functions, but* if we know cells, we know the unit from which the entire human being is constructed. That is why it is necessary for us to study histology and cellular pathology. *The reaction of the body as a whole depends upon the changes which may occur in the cell.*

Louis Pasteur (1822-1895), the diminutive French chemist, indirectly did more to make modern surgery possible than any one man. He discovered that living organisms cause putrefaction and proved the theory of "spontaneous generation" *to be a myth. He made a very important* statement that to us seems obvious—he said in effect that the germ had a

parent from which it came. His biography should be read by everyone in medicine. He was not a physician, but his careful analytical mind led him into paths that transformed the concept of medical practice. Besides determining that "sour" or spoiled wine was due to living organisms, he showed how heat and then cooling would kill these bacteria (pasteurization). He also introduced vaccine for anthrax and the method of immunization for rabies which is in use today.

Robert Koch (1843-1895) is regarded as the father of modern bacteriology. Pasteur evolved the theory and Koch discovered bacteria and practically developed the science of bacteriology. Prior to his time no methods of staining were available by which bacteria could be easily identified. He also taught us how to grow bacteria on solid media. His description and identification of the tubercle bacillus was epoch-making.

His five postulates proving that a given organism was the cause of a given disease were: (1) The microorganism must be present and demonstrable in every case of the disease; (2) it must be isolated in a pure culture; (3) inoculation from such culture must reproduce the disease in susceptible animals; (4) it must be reobtained from the animals; (5) and it must be grown again in a pure culture.

Koch thought that a vaccine could be made which would immunize an individual against the germ in every instance. He is reported to have said that an individual is more or less the victim of any bacteria he might encounter. Needless to say, in these latter concepts he erred, as Ehrlich and Metchnikoff subsequently showed by their studies in immunity.

A contemporary of Pasteur's and Koch's was the Englishman, *Joseph Lister* (1827-1912). Compound fractures were almost 90 per cent fatal in his time; today the mortality is extremely low. By using carbolic acid as an antiseptic he cut down the mortality in England from 95 to 40 per cent. He correctly predicted that the time would come when the mortality from compound fractures would be almost nil.

Nurses in that day would spray carbolic acid over the patient, the surgeon, and the room. Instruments were soaked in it. That was antiseptic surgery. Often a member of the staff or the surgeon would be overcome from carbolic acid poisoning during the course of the operation. Here we have an example of the slow and halting but persistent progress of medicine. First, as a result of Pasteur's and Koch's discoveries, bacteria were found to be the cause of suppuration in wounds; then Lister decided that he must kill these bacteria in order to get healing with a minimum of infection; then Halsted and others reasoned that it would be far better to exclude them as much as posible and thus today we have substituted so-called aseptic for antiseptic surgery.

Strictly speaking, modern surgery is not aseptic. Even after the most meticulous scrubbing and use of antiseptics the skin still harbors bacteria in the sebaceous glands and hair follicles. Only the "transient" bacteria have been removed. Furthermore, there are more bacteria in a surgical wound toward the end of an operation. These enter from the air and from the nose and the throat of the surgeons and nurses in

spite of careful masking. Experiments show also that there are more bacteria on the surgeon's hands at the conclusion of an operation than at the beginning. These facts have led to sterilization of the air in the operating room by ultraviolet light, scrubbing or débridement of the surgical wound at the conclusion of an operation, improved masks, and change of gloves (with second scrubbing) before the surgical closure.

Aseptic surgery with the aid of anesthesia (Crawford Long, 1815-1878, and Horace Wells, 1815-1848) has made modern surgery possible.

Crawford Long used ether in 1842 but he did not publish his work. Horace Wells, a dentist, used nitrous oxide in 1844. It was William T. G. Morton who persuaded John Collins Warren to try ether as an anesthetic agent on a patient with a vascular tumor just below the left jaw. This operation was successfully performed on Oct. 16, 1846.

Soporifics as a substitute for anesthesia were known to the ancients. Garrison quotes the Bible (Genesis 2:21), "And the Lord God caused a deep sleep to fall upon Adam and he slept: and he took one of his ribs, and closed up the flesh instead thereof." Opium, Indiana hemp *(Canabis indica)*, the mandrake *(Atropa mandragora)*, henbane *(hyoscyamus)*, dewtry *(Datura stramonium)*, hemlock *(Conium)*, and lettuce *(Lactuca)* were known to the Orientals and the Greeks. As early as the thirteenth century a mixture of drugs was recommended for surgical anesthesia. Man has always looked upon hell as a place of painful torture. Nothing imaginable could be worse than pain. The relief of pain has always been one of the first duties of the physician.

The *Twentieth Century* stands for preventive medicine: "Prevention is better than the cure." Today the "experimenters" (those materialists of old who wanted to reduce everything to chemistry and physics) and the clinicians (vitalists of old who leaned more toward constitutional factors) are working together for the onward progress of medicine. In surgery the more scientific the interpretation of a patient's ability to stand an operation, the less will be the necessity for invoking ill-defined constitutional factors.

MODERN SURGERY

Surgery is the treatment of malformations and disease by manual operation. It is perhaps the most important form of therapy. The surgeon must know medicine and must have manual dexterity. However, the surgeon's care does not always involve the use of the scalpel. There are times in surgical conditions when palliative measures are preferable. Corrective appliances in the care of fractures, hot fomentations in streptococcus cellulitis, drugs such as the sulfonamides, penicillin, and streptomycin, thermal and electrical agents—these belong to surgery also. Surgical operations are perhaps the most important part of surgery.

Today surgery has been divided into many different branches—orthopedic surgery, gynecology, ophthalmology, otolaryngology, traumatic surgery, neurosurgery, genitourinary surgery, etc. If we divide and subdivide the branches too much we may lose the proper perspective and arrive at the stage where "we can't see the forest because of the trees." It is well to remember that although surgery is chiefly a method

of treatment, its study includes the cause of disease (etiology), its morbid effects (pathology), and its symptoms and signs, making diagnosis and prognosis possible. It seeks to correct malformations, remove diseased tissue and foreign bodies, restore function, relieve pain, effect drainage for abnormal exudates, improve appearance; in short, it tries to restore a sick body to a normal state, as does all medical treatment. It is perhaps the "chief therapeutic resource of the physician."

A few surgical maxims that we have given medical students will summarize so-called modern trends of surgery. As the "principles" are studied, their true meaning will become apparent.

1. "A good surgeon is an internist who performs operations."

2. The more mature and accurate the diagnosis, the less a surgeon will have to explore. Therefore, careful medical and surgical diagnosis is essential.

3. Checking the surgeon to determine his speed used to be a habit among surgeons. More important is how cautious and how carefully the surgeon work—not how "fast" he is. A slow, careful operation is less apt to cause shock than one which is hurriedly and ruthlessly done in a few minutes.

4. Handle the tissues with loving kindness and they will heal in the same manner. This is a good maxim and is as important as asepsis in surgery.

5. The operative risk may be reduced by performing an operation in two or three stages if necessary.

6. There is no operation which has merit enough to be used on the patient who cannot stand it.

7. The greater the indications for surgery, the better the results.

8. Obese patients should not be subjected to abdominal operations (except in emergencies) until they have reduced.

9. Nature "in the raw" is not pleasing to our ethical or esthetic sense. However, a careful study of the manner in which animals care for their wounds may teach the surgeon that his chief function is to learn the methods of nature as best he can and to help rather than hinder her efforts.

10. When not to operate upon a patient is as important to know as when to intervene.

11. Cautiousness is the byword of the surgeon.

12. All operations may be dangerous to life and may be followed by distressing aftereffects.

13. Operations are to be avoided in hysterical or mentally deranged persons except when absolutely necessary.

14. The surgeon must never minimize the dangers of surgery; he should not "sell" an operation to a patient, and he must not promise that which is impossible or at most improbable.

15. The modern trend of surgery is toward conservatism.

16. Functional disease is made worse by calling a patient's attention to it.

17. The tacit or implied request of a patient on the operating table is: "My life is in your hands—be cautious; use all the skill, knowledge, and acumen you possess to cure me if possible and give me back to my loved ones."

The student will do well to learn the basic principles thoroughly; then these may be applied to any branch. They form the broad foundation upon which any superstructure may be built. This book is written with this thought in mind.

METHODS OF MODERN SURGERY

Preoperative Preparation.—The surgical operation really begins in the preparation of the patient for an ordeal. It is the surgeon's duty to evaluate the risk of the operation and to determine whether or not the patient is equal to it. He is pitting his skill, knowledge, and the operation against the ravages of the disease and the patient's ability to stand the surgery. Accurate diagnosis of the lesion to be attacked and of the patient's condition as a whole is necessary. Special states such as diabetes, dehydration, anemia due to blood loss, *alkalosis, acidosis, cardiovascular* renal disease, liver damage, and avitaminosis demand attention.

The Operation.—In performing the surgical operation the surgeon must be able to recognize diseased tissues by sight and touch; he must understand repair, the effects of bacterial invasion, the devastating effects of new growth and their method of dissemination. Moreover, in his efforts to remove diseased tissue, he must not lose sight of the patient's ability to withstand extensive procedure.

Thorough study and preparation of the patient and extreme care in the conduct of the operation will usually prevent untoward effects from the operation itself.

Postoperative Care.—This includes a continuance of measures instituted preoperatively and requires of the surgeon an intimate knowledge of wound healing, the effects of hemorrhage and shock, anoxemia, acido*sis, alkalosis, water balance, salt and protein metabolism, measures to* prevent thrombosis and embolism, urinary infections and lung complications, perversions in motor activity of the gastrointestinal tract, and the causes of postoperative fever. *A consideration of these entities will be* found in this book.

In the early years of surgery mortality was the surgeon's chief concern. Today a minimum mortality is taken for granted and the surgeon looks not only to the immediate recovery of the patient, but to his permanent cure as well. By a follow-up system he is able to evaluate the merits of his work.

A careful study of the natural course of a disease is important in evaluating the *efficacy of surgical treatment.* Perhaps nature can do more than the surgeon.

The surgeon, like the physician, has as his chief function, then, the saving of life and the restoration of health. To accomplish this he must have *surgical judgment.* This is based upon an accurate knowledge of surgical pathology and the fundamental principles of surgery.

The following is an outline of some of the more important considerations in operative surgery:

A surgical operation is an experiment in which the knowledge and skill of the physician is pitted *against the ravages* of the disease. It is his duty to evaluate the

patient's ability to stand surgery and to prepare him for the ordeal. He must be meticulous in the conduct of his operation and then meet the requirements necessary to assure recovery after the operation is over.

Aphorism—There is no operation that has merit enough to be used on a patient who cannot stand it

Preparation for Surgery—Preoperative Care

A. General considerations

Aphorism—Surgery demands careful attention to details

1. How does the patient vary from the normal
   a. Due to his disease
   b. *Due to his deficiencies caused by (1) the disease and (2) complications*
      If the patient is absolutely normal, very little preparation is necessary; if greatly abnormal, much treatment will be required
2. What are normals
   a. The ability to inhale and utilize oxygen
      Types of anoxia:
      (1) anoxic
      (2) anemic
      (3) stagnant
      (4) histotoxic
      (5) combinations
   b. The ability to make blood, retain it, and maintain an adequate circulation
      Causes of blood deficiency and circulatory failure:
      (1) Disease of the blood forming organs
      (2) excessive loss of blood
      (3) the disproportion between volume of circulating blood and vascular bed
   c. The ability to eat and drink and assimilate food and water
      The body contains 70 per cent of water: 50 per cent intracellular, 15 per cent intercellular, and 5 per cent intravascular; the labile portion is the intercellular component
      (1) The amount of water depends on the amount of sodium
      (2) The amount of sodium is always in isotonic concentration with the amount of potassium in the cells
      (3) The cell membranes are impermeable to cations but not to anions
      (4) There is a free interchange of electrolytes between the vascular tree and intercellular spaces

Aphorism—The alimentary canal and not the veins were made for eating and drinking; underhydration is better than overhydration

   d. *The ability to eliminate waste products through kidneys,* bowels, and lungs and thus maintain a normal acid base balance
      Acid base balance is important and closely related to water balance
      (1) the only base is that which is ingested
      (2) acids are constantly being formed by the body
      (3) the control of this balance is related to two factors:
         (a) chemical, which are the buffers of the blood

(b) physiological, which are the means of eliminating excessive amounts of acids or base by the lungs or kidneys; fluids and chemicals are used in an effort to keep the balance as nearly normal as possible.

Aphorism—Acidosis is better than alkalosis

e. The ability to withstand infection by healthy antibody system

(1) the age of antiseptics is gone

(2) chemotherapeutic agents act by making the environment unfavorable for bacterial growth

(3) Antibiotics interfere with reproduction of bacteria

(4) No therapeutic agent cures infection; this is accomplished by healthy, active cells and antibodies

f. The ability to withstand the nervous strain of anesthesia and surgery

Barbiturates should be used with great caution

(1) They are respiratory depressants and many individuals are sensitive to them

(2) Morphine in small doses with atropin is still an excellent combination

(3) Demerol is useful in chest surgery because it is less depressive to the respiratory center

Conduct of Operation

A. Anesthetic

1. Oxygen requirement met by
   a. Open airway
   b. Endotracheal tube in chest surgery especially
   c. Oxygen administration
   d. Automatic respiration
   e. Elimination of carbon dioxide

B. Fluids needed, depending on

1. Degree of subhydration prior to surgery
2. Amount of sweating and length of operation to make up insensible water loss

C. The amount of blood lost in surgery is difficult to estimate; many methods are in use

1. The use of dry sponges and weighing them
2. Colorimeter
3. Standard scales of blood loss for various operations
4. Hematocrit, hemoglobin, red blood count, and plasma protein determinations are useless because hemodilution does not occur until two hours or more after the blood has been lost
5. Best guide is blood pressure and pulse rate together with a knowledge of approximate amount of blood lost in any particular operation

Postoperative Care

How has the operation affected the condition of the patient? If not at all, relieve pain and nothing more.

Aphorism—Excessive treatment is an unnecessary burden to patient and may have serious consequences

Consider:

1. Interference with oxygen consumption and utilization
2. Loss of blood and fluid

3. Contamination which may lead to infection
4. Ability to eat and drink and assimilate food and water
5. Ability to eliminate water through kidneys; Anuria: prerenal, renal, and postrenal
6. Pain and nervous strain
7. Enervating effects of prolonged bed rest and possible complications (thromboembolism, lung complications, bladder complications, bowel distention) are, to a large extent, obviated by early mobilization

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Chapter 2

PATHOLOGY

Pathology is the study of disease, its causes, manifestations, and effects. It is always changing, always new. Although it deals chiefly with morphological changes, it is inextricably linked with altered physiological processes. The modern clinical pathologist is a consultant who helps in the diagnosis and treatment of disease.

A study of the normal (anatomy and histology) must precede the study of the abnormal (pathology). By careful examination of the patient an attempt is made to diagnose his ailment, and then if an operation is performed or if tissue is removed for biopsy, it must be carefully examined. In this way we learn how to interpret clinical symptoms and signs in the light of pathological changes.

Gross Pathology.—Gross pathology is studied at the (1) surgical table and at (2) autopsy.

Medical students must witness and perform many autopsies, because here the effects of disease are best learned. The surgeon must observe and handle diseased tissue so that he may recognize with his hands as well as his eyes the gross characteristics of disease.

Microscopic Examination.—Lesions may be studied in sections of tissue from (1) autopsy, (2) surgery (frozen section and paraffin sections of tissue and organs removed), (3) biopsy, and (4) living tissue—vital and supravital staining.

Frozen Section.—The microscope is indispensable for detailed study. Very often the surgeon performs an operation on a patient with a new growth and he cannot be sure from gross appearance whether it is a malignant or benign neoplasm. The pathologist makes a frozen section and examines the growth under the microscope. In fifteen or twenty minutes he can usually tell whether it is a malignant lesion which requires radical and extensive surgery or a benign growth for which local excision will suffice. Many of the more common neoplasms will be discussed later in our text. We shall also consider the history and findings in the case and thus reconstruct the entire clinical as well as pathological picture.

Biopsy.—A patient may have a swelling which may be a cyst or an enlarged lymph gland or an infectious process. The diagnosis may be extremely difficult. The surgeon may remove the lymph gland or edge of the ulcer and submit it to the pathologist and a diagnosis may be made in this way. This is known as surgical biopsy. The term implies both the removal and examination of the tissue. Another form is the needle biopsy; some cells from the diseased tissue are aspirated into a

hollow needle after making a small incision. The specimen is then spread on a slide and studied under the microscope. This is especially helpful in the diagnosis of brain tumors.

Vital Staining.—A small incision is made over the sternum. A large needle and syringe are used to aspirate some bone marrow for study. This procedure is employed in the diagnosis of anemias and leucemias. Some fatal cells are not seen normally after birth; other cells are found only in bone marrow. In blood dyscrasias marrow cells may be found in the circulating blood and very primitive cells in the marrow.

Supravital staining has to do chiefly with certain "reticulated" red corpuscles, which contain a coarse skein or network of granular filaments. This is an attempt to stain the blood cells in the living state by the administration of certain dyes.

***Examination of Microorganisms and Cells Causing or Complicating* Disease.**—

Exudates (Pus or Serum).—Exudates are composed of the fluid and cellular parts of the blood and tissues and occur as a result of active hyperemia in response to an injury (bacterial, mechanical, or chemical). This implies that insofar as blood constituents are concerned they have been permitted to leave the capillaries as a result of increased permeability. Transudates are composed of the fluid parts of the blood with some cells. They traverse normal capillaries and vary in amounts and consistency in different parts of the body, depending upon slight variations in capillary permeability. Although not produced by active hyperemia, they are nevertheless affected by the hydrostatic and osmotic pressures which prevail. If, however, as a result of anoxemia, capillary walls become affected, transuding fluid becomes an exudate. Based upon this definition, ascites and edema of the extremity due to occluded veins or lymphatics would be classed as exudates, whereas edema due to hypoproteinemia as seen in nephrosis or starvation states would be called transudates.

Smears are usually made by dipping an applicator with cotton into the exudate and then lightly stroking a glass slide; for example, a smear from the throat to determine whether or not diphtheria is present, or from the urethra for gonorrhea. These same exudates may be cultured in test tubes to see if the bacteria will grow so that they may be definitely identified. Recently tryspin has been used to digest the material so that the tubercle bacillus may be more easily stained and identified. If in extreme doubt, some of the material from the lung or pleural cavity, for example, is injected into a guinea pig, an animal that is extremely susceptible to tuberculosis. In about ten days if the fluid contains tubercle bacilli the guinea pig will die of tuberculosis, or it may be sacrificed sooner and show tuberculosis at autopsy. In suspected carcinoma deciduous cells are sought by centrifuging the exudate and staining the smear.

Blood and the Other Body Fluids.—If a patient l for example, blood smears may show the presence of site. From the same patient a blood culture may be n withdrawn and incubated on different media; if it show bacterium may be identified. This is especially imp fever and also in undulant fever, where we depend alm blood culture and agglutination tests for diagnosis.

The examination of urine and stool cultures in pat rhea is important. This is especially true in typhoid fe amoebic dysentery (stool), for parasites and ova. Carc also searched for in suspected cases. This is especially tr of the kidney or bladder (urine cells).

Serology.—Wassermann, Kahn, Kline, or Mazzini b *syphilis should be routine. Often it is necessary to make th* on the blood and spinal fluid.

Colloidal gold curve is of aid in the diagnosis of pares cerebrospinal diseases.

Allergic phenomena. Certain allergic states, such as hay fever, defy successful cure unless the causative agent is by skin tests.

Chemical Examination of Blood, Urine, Feces, Gastric Ju

Blood.—The calcium content of the blood is important in roidism, the carbon dioxide combining power in acidosis and oxygen determination in anoxemic states and arteriovenous nonprotein nitrogen and uric acid in azotemic states produced by tis, etc., blood sugar in diabetes, and serum globulin and alb edema.

Urine.—Abnormal constituents are sugar, acetone, and diacet in diabetes, albumin in nephrosis, bile in obstructive jaundice, etc.

The *Friedman* test for pregnancy is done by the injection of t tient's urine into an immature female rabbit's ear; the animal is sacrificed and the tubes and ovaries are examined for maturation o follicles. The *Aschheim-Zondek* test, which was the original test for p nancy, is now used for the quantitative determination of the gonadotr hormone. Immature female mice are used and the results expressed mouse units per liter.

Feces.—Tests for blood, occult blood (blood that is not visible to the naked eye), undigested fats, etc., are available.

Gastric juice may be tested for the amount of free hydrochloric ac and combined acid. This is a great aid in the diagnosis and treatment of peptic ulcer (high acid) and pernicious anemia (achlorhydria).

Cytologic Examinations.—

Blood.—Leucocyte, erythrocyte, and Schilling counts and various specific cells are listed on the laboratory sheets. Normally, immature

polymorphonuclear leucocytes make up about 10 per cent of the total differential count. In infections the blood sends out the white cells in great numbers. Schilling counts record the number of immature cells (band cells, myelocytes, and metamyelocytes); if these are present in large number, 20 to 30 per cent, a "shift to the left" is said to have occurred. This is seen in acute sepsis, appendicitis, etc., and implies that the body is not keeping pace with the infection and is sending out untrained "soldiers." A "shift to the right" means that the blood is fighting with its adult white cells and is combating infection successfully.

If the blood count showed 80,000 white cells, the surgeon would think of leucemia rather than infection although pertussis in infants may produce extreme leucocytosis (mostly lymphocytes). Therefore, cell counts are done routinely on all patients who enter the hospital. The significance of this will be more apparent when the subject of infection is discussed in Chapters 3 and 4. Thrombocytes (blood platelets) are counted in all hemorrhagic states. This test is used in the diagnosis of thrombocytopenic purpura.

Cytologic examination of *pus* and other *exudates* is important to the surgeon because it tells him the type of infection he is dealing with. The serosanguineous exudate of the streptococcus and the thick creamy purulent exudate of staphylococcus are more or less characteristic. If he looks at fluid from the pleural cavity and it contains pus cells, it is probably an empyema; if it is clear except for a few lymphocytes, it probably is tuberculosis; if many red blood cells are found in the exudate, cancer of the lung may be present. Cancer cells may be found by centrifuging and making a "button" and then staining with hematoxylin and eosin stain; or a saturated aqueous solution of picric acid may be used, the tissue desquamations fixed in paraffin blocks, and then cut and stained with hematoxylin and eosin.

The Papanicolaou technique consists of placing the exudate on slides, immersing them in ether and 95 per cent alcohol (equal parts), leaving the slide in this mixture for one to twenty-four hours, depending on when the stains can be made, and then staining with the Papanicolaou polychrome stain. If the smear is to be sent away, the slide should be covered with glycerin.

Metabolism Tests.—Metabolism is a term used to include the different chemical processes which occur in the tissues. Growth and heat production depend on these processes, and energy for muscular activity and vital functions is derived from them.

The basal metabolic rate means the basal amount of energy that is used by the patient. Basal in the sense that the patient is at complete muscular and mental rest and in the postabsorptive state, twelve to fourteen hours after a meal when digestive processes are over. It is found by measuring oxygen consumption. The test properly done and interpreted is especially useful in the diagnosis and treatment of toxic goiter.

Blood and the Other Body Fluids.—If a patient has chills and fever, for example, blood smears may show the presence of the malaria parasite. From the same patient a blood culture may be necessary. Blood is withdrawn and incubated on different media; if it shows any growth, the bacterium may be identified. This is especially important in typhoid fever and also in undulant fever, where we depend almost entirely upon blood culture and agglutination tests for diagnosis.

The examination of urine and stool cultures in patients with diarrhea is important. This is especially true in typhoid fever (urine) and amoebic dysentery (stool), for parasites and ova. Carcinoma cells are also searched for in suspected cases. This is especially true in carcinoma of the kidney or bladder (urine cells).

Serology.—Wassermann, Kahn, Kline, or Mazzini blood tests for syphilis should be routine. Often it is necessary to make these tests both on the blood and spinal fluid.

Colloidal gold curve is of aid in the diagnosis of paresis and other cerebrospinal diseases.

Allergic phenomena. Certain allergic states, such as asthma and hay fever, defy successful cure unless the causative agent is determined by skin tests.

Chemical Examination of Blood, Urine, Feces, Gastric Juice, Etc.—

Blood.—The calcium content of the blood is important in parathyroidism, the carbon dioxide combining power in acidosis and alkalosis, oxygen determination in anoxemic states and arteriovenous fistulas, nonprotein nitrogen and uric acid in azotemic states produced by nephritis, etc., blood sugar in diabetes, and serum globulin and albumin in edema.

Urine.—Abnormal constituents are sugar, acetone, and diacetic acid in diabetes, albumin in nephrosis, bile in obstructive jaundice, etc.

The *Friedman* test for pregnancy is done by the injection of the patient's urine into an immature female rabbit's ear; the animal is later sacrificed and the tubes and ovaries are examined for maturation of the follicles. The *Aschheim-Zondek* test, which was the original test for pregnancy, is now used for the quantitative determination of the gonadotropic hormone. Immature female mice are used and the results expressed in mouse units per liter.

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Cytologic Examinations.—

Blood.—Leucocyte, erythrocyte, and Schilling counts and various specific cells are listed on the laboratory sheets. Normally, immature

Leucocytes

Men, 5,000 to 10,000 per cubic millimeter of blood

Women, 5,000 to 10,000 per cubic millimeter of blood

Differential count

	RELATIVE VALUES (%)	ABSOLUTE VALUES (PER C.MM. OF BLOOD)
Neutrophils	60-70	3,000-7,000
Basophils	0.5-1	0- 100
Eosinophils	1-3	50- 300
Immature cells		
Myelocytes	0	
Metamyelocytes	2-4	
Band cells	4-10	
Lymphocytes	20-40	1,000-4,000
Monocytes	2-6	100- 600

Color index, 1.0

Volume of packed cells (Wintrobe hematocrit method)

Men, 46 c.c. per 100 c.c. of blood

Women, 42 c.c. per 100 c.c. of blood

Average figure for both sexes, 42.4 per 100 c.c. of blood

Volume index, 1.0

Saturation index, about 1.0

Mean corpuscular hemoglobin, 27 to 32 micromicrograms

Mean corpuscular hemoglobin concentration, 32 to 38 per cent

Mean corpuscular volume, 80 to 94 cubic micra

Reticulocytes, 0.1 per cent of erythrocytes

Thrombocytes platelets

250,000 to 350,000 per cubic millimeter of blood

1 platelet for every 20 erythrocytes (Fonio's smear method)

Coagulation time

2 to 6 minutes (slide method)

3 to 8 minutes (capillary tube method)

5 to 10 minutes (Lee and White's method—venous blood in test tube method)

Bleeding time

2 to 3 minutes

Clot retraction time

Beginning retraction in 1 to 6 hours

Complete in 24 hours

Resistance of erythrocytes to hypotonic salt solutions (fragility test)

Beginning hemolysis from 0.44 to 0.42 per cent NaCl

Complete hemolysis from 0.34 to 0.42 per cent NaCl

Icterus index, 1 to 5

Van den Bergh reaction

Indirect reaction—Normal serum contains 0.1 to 0.3 mg. bilirubin per 100 c.c. of blood

Sedimentation rate

Men, 0 to 8 mm. in 1 hour

Women, 0 to 2– mm. in 1 hour

Sheep cell agglutination, not above 1.8 dilution

Experimental Pathology.—Occasionally we read of the activities of a strange organization called the antivivisection society. This group would prevent all vivisection. This attitude, if carried out, would delay the progress of medicine materially. Such diseases as cancer, heart disease, leucemias, endocrine dyscrasia, etc., must be conquered through experiments on lower animals.

This is the great uncharted and unknown field of pathology. Abnormal states are purposefully induced in animals so that they may be accurately studied as to their cause *and pathological changes in the hope* that successful treatment will follow. Such conditions as shock, burns, intestinal obstruction, peptic ulcer, lung abscess, empyema, etc., have been produced in experimental animals and, as a result, the treatment of *these conditions in the human being has been greatly improved.*

In summarizing the value of pathologic tests we may say that some of them are so important as to be routinely required (blood counts, urinalysis, and Kline and Mazzini tests); others are needed to help establish *the diagnosis, to guide in treatment, or to help in prognosis.* In a few instances they are diagnostic; in many they must be viewed in the same light as any other symptom.

Certain laboratory work is routine and indispensable. For example, a child comes to the hospital with suspected appendicitis. A routine blood count and urinalysis are done. This helps in diagnosis, prognosis, and treatment.

Routine urinalysis may reveal a pyelitis or diabetes which may simulate appendicitis. A concentrated urine with acetone indicates dehydration and acidosis which requires treatment before any operation can be performed. (See Chapters 11 and 12.)

Routine leucocyte counts may reveal an unsuspected leucemia. The acuteness of the infection (Schilling count) is revealed and a more accurate prognosis may be given (Walker index). (See Chapter 4.) A very high hemoglobin and red blood cell count *(hemoconcentration) indicates dehydration, showing that* a loss of plasma has occurred (due to starvation, vomiting, or diarrhea or diffuse inflammation of the peritoneum). (See Chapters 11 and 14.) This requires blood transfusion. Plasma proteins and hemoglobin and hematocrit values are important in the treatment of shock and dehydration. These may be determined quickly by the copper sulfate method for measuring specific gravities of whole blood and plasma.

In this way errors in diagnosis are minimized and proper preparation of the patient is possible before surgical intervention. This is more important in complicated appendicitis than the time of operation.

The *following is a list of normal values for laboratory determinations* which has been compiled from various sources and from experience with tests done at the Indiana University Medical Center.

Blood—Adults

Hemoglobin (Newcomer's method)

Men, 14.5 to 16.9 Gm. per 100 c.c. of blood
Women, 12.5 to 15.0 Gm. per 100 c.c. of blood

Erythrocytes

Men, 4.5 to 6.0 million per cubic millimeter of blood
Women, 4.0 to 5.6 million per cubic millimeter of blood

TABLE I

GROUP				SERUM	SERUM OF GROUP	RED BLOOD CORPUSCLES OF GROUP				PER CENT OF ADULTS IN EACH GROUP
LANDSTEINER	MOSS	JANSKY	CORPUSCLES			AB	A	B	O	
AB	I	IV	Agglutinogens AB	Agglutinin o	AB; that is, agglutinin o	–	–	–	–	7
A	II	II	Agglutinogen A	Agglutinin b	A; that is, agglutinin b	+	–	+	–	40
B	III	III	Agglutinogen B	Agglutinin a	B; that is, agglutinin a	+	+	–	–	10
O	IV	I	Agglutinogen O	Agglutinins ab	O; that is, agglutinin ab	+	+	+	–	43

+, Hemoagglutination; –, no hemoagglutination.

Blood Groups

Transfusion *reactions occur* because of hemolysis or agglutination of the donor's or recipient's cells or both. *Since hemolysis does* not occur without agglutination, the latter is observed in blood *matching. Two factors are involved in this* process: agglutinins in plasma and agglutinogens in cells.

Landsteiner's four basic groups *are based on two isoagglutinins* in serum, designated as a and b, and two isoagglutinogens *in cells, designated as A and B. In* Table I is a classification of the four blood groups of Landsteiner, *Moss, and Jansky* and their antigenic analyses.

It is apparent that group A agglutinogen could not harbor an agglutinin or its own cells would be agglutinated. Thus a person of group A has b agglutinins. Such an individual may receive the corpuscles of his own group or of group O. A person of group B may receive group B or group O blood, but one with group O blood may receive cells from only his own group. Persons of group AB may receive corpuscles from any group but may give only to their own group.

In transfusions the important fact to remember is that the donor's cells must not contain isoagglutinogens which will be agglutinated by the isoagglutinins of the recipient's serum. Since type O has no isoagglutinogens, persons of this type may be used as universal donors. Type O serum contains isoagglutinins ab which, when transfused into the recipient slowly, are not present in high enough titer to clump *the recipient's cells. Furthermore*, much of the serum so given is quickly lost. (See Chapter 13.) *Persons of type AB may be used as universal recipients since their serum contains no isoagglutinins. However, it is best that cells and sera be cross-matched* and that same types be used if possible. Many subgroups have been established (A_1 or A_2, A_1B or A_2B) which are not important in everyday practice. (For heredity of blood groups, see Chapter 10.) Infused erythrocytes survive almost as long as those made by the recipient provided there are no incompatabilities. Their ability to take on all functions of the recipient's erythrocytes is not fully understood.

Compatability tests are not required for plasma transfusions. Indeed many donors may be used, of different blood groups, for plasma powder. The dehydrated plasma is diluted to isotonicity with distilled water or distilled water and glucose or saline solutions and immediately used in the treatment of shock and hemorrhage (q.v.). Reactions are not uncommon from reconstituted plasma and the dangers of homologous serum jaundice which are present *in all transfusions are even more prevalent following the use of plasma powder obtained from various donors.*

An individual's serum *may agglutinate* its own corpuscles when the blood is *cooled. This is said to be due to cold autoagglutinins, not isoagglutinins. Agglutinogens* other than those mentioned include M and N factors. There are no normal isoagglutinins for them in human blood and therefore they are not important in ordinary typing. Fifty per cent of the white population are of type MN, 30 per cent are of type M, and 20 per cent are of type N. Tests for M and N agglutinogens may be useful in paternity disputes since they are dominant characteristics. Still other agglutinogens and agglutinins may be associated with liver damage *or may be bacterio*genic. Repeated transfusion from the same person *may cause reactions due to* agglutinogens in small *amounts which act as antigens, stimulating* the formation of agglutinins.

Rh Factor.—If red blood corpuscles of the *Macaca rhesus* monkeys are injected *into rabbits or guinea pigs,* agglutinins develop against them. These agglutinins will also agglutinate the blood of 85 per cent of human beings regardless of isoagglutinin groups. Fifteen per cent lack this agglutinogen which is responsible for the reaction and which has been termed the Rh factor. Many atypical reactions are probably due to transfusions given an Rh-negative person with agglutinins *for corpuscles containing* the Rh factor. These agglutinins arise usually under *the following conditions:* (1) Patients who have had one *or more previous transfusions* from the same group or universal donor group; (2) *first* transfusions in a pregnant woman or recently post-

cells are frequently encountered in the blood of infants and children. Cellular immaturity in the blood of children is not always considered of serious import but indicates an instability of the embryonic hematopoietic system.

Blood Chemical Constituents and Miscellaneous Data

Nonprotein nitrogen (Made of urea N, uric acid, creatinine, amino acid N, creatine, undetermined N), 25 to 40 mg. per 100 c.c. of blood

Urea nitrogen, 18 to 35 mg. per 100 c.c. of blood

Uric acid, 1 to 3 mg. per 100 c.c. of blood

Creatinine, 1 to 2 mg. per 100 c.c. of blood

Urea clearance, 80 to 120 per cent of accepted normal excretion

Sugar, 80 to 200 mg. per 100 c.c. of blood

Chlorides

Plasma, 570 to 600 mg. per 100 c.c.

Cells, 285 to 300 mg. per 100 c.c.

Calcium

9 to 11.5 per 100 c.c. in the plasma of adults

Slightly higher (10 to 12 mg. per 100 c.c.) in that of children

	PLASMA	WHOLE BLOOD	CELLS
Magnesium	2.7 mg. per 100 c.c.	4 mg.	6 mg.
Sodium	340 mg. per 100 c.c.	160 mg.	0
Potassium	18 to 22 mg. per 100 c.c.	200	420

Iodine, 1.001 mg. per 100 c.c. plasma

Serum protein—Total, 6 to 8 Gm. per cent

Albumin, 4.5 to 5.5 Gm. per cent

Globulin, 1.5 to 3.0 Gm. per cent

Fibrinogen, 0.27 Gm. per 100 c.c.

Albumin-globulin ratio, 1.5 to 3.5

Colloid osmotic pressure, 290 to 430 mm. H_2O

Specific pressure (pressure per gram per cent of protein), 15 to 54 mm. H_2O

Specific gravity is the ratio between the density of a body and the density of a standard substance, usually water.

Plasma specific gravity: 1.027

Whole blood specific gravity: 1.060

Blood viscosity is 5 to 6 times the viscosity of distilled water (distilled water as unit).

Plasma viscosity is 1.8 to 2.1 times the viscosity of distilled water.

Bromide

Less than 50 mg. per cent. Normally none is present. Less than 50 mg. is usually of no clinical significance during its administration.

Oxygen

Arterial, 15 to 20 volumes per cent

Venous, 10 to 18 volumes per cent

Free CO_2 is 1/20 of plasma bicarbonate or 2.5 to 3.5 volumes per cent

CO_2 combining power of the plasma

55 to 80 c.c. of carbon dioxide per 100 c.c. of plasma (venous); arterial, 45 to 55 per cent

In children, 40 to 55 c.c. of carbon dioxide per 100 c.c. of plasma (venous)

Blood diastase

70 to 200 mg. of sugar per 100 c.c. can be converted from starch

Cholesterol, 150 to 200 mg. per 100 c.c. of blood

partum mother. Here the mother is Rh negative but the fetus has corpuscles which are Rh positive inherited from his Rh-positive father. A mother's red blood corpuscles may have no Rh agglutinogen. Due to leakage of agglutinogens *from the fetal circulation into the mother's circulation, agglutinins may form* in the mother against the cells of the fetus. Also an Rh-negative mother may have one or more Rh-positive offspring without a state of isoimmunization. Since an Rh-negative female who is immunized remains potentially sensitized throughout life, it is *important to test all female patients* for the Rh factor. If they are *Rh negative, they should receive* Rh-negative blood. (3) *Rarely* reactions occur with a first transfusion although there is no history of previous sensitization by transfusion or pregnancy.

The importance of this factor in pregnancy is obvious. *The mother's agglutinins in her serum against the corpuscles of the* Rh-positive fetus may enter the fetal circulation, destroying the corpuscles of the child. This results in a hemolytic anemia known as erythroblastosis fetalis. There are three clinical types: (1) Hydrops fetalis, a rare form characterized by anasarca and enlargement of the liver, spleen, and heart; *the fetus is usually stillborn or dies shortly after birth.* (2) Icteris gravis neonatorum. There is an increasing jaundice with purpura. Recovery may occur. Normal human serum or whole blood was formerly given intramuscularly. Transfusions are better. Most observers believe that Rh-negative blood should be used because the fetus has agglutinins against Rh-positive blood. Small transfusions, *40 to 60 c.c., should be slowly administered. Another method of giving blood is replacement transfusions, using* the umbilical vein. *Long plastic cannulas* are employed and *30 c.c.* are given, *then 30* c.c. withdrawn, until the blood volume has been replaced (350-500 c.c.). Vitamin K is also given. (3) Hemolytic anemia of the newborn, which may occur without erythroblastemia and without hydrops or jaundice. The spleen is enlarged. Treatment is the same as for icteris gravis neonatorum. *Rh factor subgroups* consist of Rh_o, Rh′, Rh″. Eighty-five per cent of Caucasians possess the Rh_o factor along with one or both the others; *3½ per cent possess only one factor;* and 13 per cent lack all three factors (Rh negatives).

Blood—Children

Erythrocytes, leucocytes, platelets, and hemoglobin values are *high at birth.* The following normal values are given by Blackfan and associates for normal newborn infants:

Hemoglobin, 95 to 140 per cent
Erythrocytes, 5 to 8 million per cubic millimeter of blood
Leucocytes, 15,000 to 25,000 per cubic millimeter of blood
Platelets, 200,000 to 400,000 per cubic millimeter of blood

With the first three months there is a physiological decrease in red cells and hemoglobin (the latter frequently falling to a level of as low as 65 to 75 per cent) which is explained by Davidson and Leitch as the result of two factors:

1. A decrease in *bone marrow activity due to the high* oxygen tension of extrauterine life and
2. A destruction of erythrocytes by hemolysis. *The red cell and hemoglobin* values rise until the normal level is reached about the sixth month.

The differential count likewise is altered during infancy. There is a neutrophilia *immediately after* birth which gradually recedes to 25 to 50 per cent during the first *two weeks. Following* this period there is a gradual increase of 40 to 60 per cent during the next five or six months, but a normal level is not attained until about the twelfth year. This relative *decrease of neutrophils* between the second week and the twelfth year is accompanied *by a slight relative and* absolute lymphocytosis. Eosinophils, basophils, and monocytes *occur soon after birth in higher* numbers than in adults, but normal levels are usually reached *at the end of two weeks. Immature* red and white

Gastric Acidity

Free HCl 25 to 50 (25 to 50 c.c. N/10 HCl per 100 c.c. gastric juice)
Acid per cent
Total acidity, 50 to 75 acid per cent
Gastric mucin, 0.4 to 0.7 mg. per 1 c.c. of gastric juice

Basal Metabolic Rate

Plus 15 to minus 15

CLASSIFICATION OF DISEASE FROM THE STANDPOINT OF THE PATHOLOGIST

1. *Degenerative or involutional diseases*
   Examples: Arteriosclerosis, cataract, atrophies of organs, gangrene due to arteriosclerosis, fractures due to osteosclerosis, etc.
2. Congenital malformations and abnormalities
   Examples: Cleft palate, harelip, clubfoot, hernia, etc.
3. Trauma or affections caused by injurious contact between the body and its environment
   Examples: Burns, frostbite, fractures, wounds, poisonings, etc.
4. Deficiency diseases or absence of essential nutritional substances due to:
   a. Environment (starvation, wrong foods, lack of vitamins, etc.)
   b. *Inability to absorb food (gastric carcinoma, duodenal fistula, etc.)*
   c. Inability to metabolize (pernicious anemia, diabetes, etc.)
5. Disorders of metabolism
   Chemical processes take a perverted course or are incomplete
   Endocrine disorders such as diabetes, gout, obesity, hyperthyroidism, etc.
   Allergy
6. Neoplasms
7. Diseases caused by animal parasites
8. Diseases caused by living microorganisms
   Bacteria and fungi
9. Diseases caused by filtrable viruses
10. Obstruction to principal ducts or outlets of organs
    May result from diseases listed under numbers 2, 3, 6, 7, 8, and 10
    Intestinal, common bile duct, ureter, etc.

This list will undoubtedly be changed as new discoveries are made and a better understanding of diseases is evolved. The surgeon should have a general outline of disease which he may apply in a practical manner. Very often it will be difficult to categorize an illness without lab-

Cholesterol esters, 110 to 145 mg. per cent
- Lecithin, 200 to 250 mg. per cent
- Lipase, 0.2 to 1.5 c.c. N/20, Na OH for each cubic centimeter
- Lipids, 650 to 750 mg.

Phosphorus (inorganic)
- Adults, 2 to 5 mg. per cent
- Children, 4 to 7 mg. per cent

Phosphatase, 1.5 to 5 (Bodanski units)

Rose bengal test, 80 to 120 per cent of normal excretion

Bromsulphalein test
- At 5 minutes 20 to 50 per cent retention
- At 30 minutes, no retention
- Less than 15 per cent should be retained at the end of 1 hour

Blood volume, 90 c.c. per kilogram of body weight; *plasma volume*, 50 c.c. per kilogram of body weight

Blood *sulfanilamide*
- Should not exceed 10 mg. per cent while being administered

Blood sulfapyridine
- Should not exceed 8 to 12 mg. per cent while being administered

Sulfadiazine, 10 to 12 mg. per cent

Sulfathiazole, 5 to 8 mg. per cent

Thiocyanate, 6 to 10 mg. per cent

Blood ascorbic acid, 1.5 to 2.0 mg. per 100 c.c. of blood plasma

Prothrombin
- Expressed in per cent of normal control; about 35 mg. per 100 c.c. of whole blood
- Prothrombin levels below 50 per cent of normal may be accompanied by bleeding. This is seen in obstructive jaundice and cirrhosis of the liver. Although this is extremely variable and the bleeding tendency may not be present when only 20 per cent of normal is present, it may occur with prothrombin levels of 70 to 80 per cent of normal. This is explained by the small or large reserve of prothrombin which may be present. Vitamin K is not a part of the prothrombin molecule. It aids in its synthesis

Urine

P. S. P. test
- 15 minute specimen, 25 per cent or above
- 30 minute specimen, 15 to 20 per cent

Galactose tolerance test
- Patient should not excrete more than 1.5 Gm. in the five-hour period following ingestion

Urobilin, 0.5 to 2 mg.

Spinal Fluid

Spinal fluid sugar, 40 to 60 mg. per cent

Spinal fluid protein, 20 to 40 mg. per cent

Colloidal gold curve
- Normal, 0000000000
- Meningovascular neurosyphilis, 0244310000
- Paresis, 5554321000
- Brain tumor and tuberculous meningitis, 0000123100
- Meningitis other than tuberculous, 0000012334

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oratory aid. Sometimes even then such classification may be untenable. In general, the following guide may be used:

1. That with which the individual is born (congenital malformations)
2. That which he naturally develops as he declines (degenerative or involutional diseases)
3. That which has to do with perverse functional activities of the body
   a. Chemical—secretions and excretions abnormal in amount or kind
   b. Mechanical activity—abnormal in amount or action
   c. Disorders of metabolism
4. That which is caused by injurious contact with his environment
   a. Physical and psychic
   b. Germs and animal parasites
   c. Food
      Too much
      Too little (starvation states)
      Improper kind (vitamin deficiencies)
5. Circulatory disturbances
6. Neoplasms

The treatment of disease may be outlined as follows:

Functional disorders

1. Amenable to nonsurgical methods
2. Demands surgical intervention to prevent organic change or to alleviate disfunction

Organic disease

1. Self-limited and better treated symptomatically
2. May be treated by drugs or nonoperative methods
3. Surgery indicated for cure
4. Morbid changes too far advanced for cure
5. Palliative procedures desirable

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permeable membranes. A homogeneous, pore-free masslike gelatin and most proteins absorb liquids, undergoing an increase in volume—this is called molecular imbibition (Fick).

Serum is the liquid part of the blood which separates after coagulation; chemically it is blood plasma from which the fibrinogen has been removed by coagulation. The scab which results from hardened serum is due to a process known as syneresis. All surface films have a contractile action. It is this contractile action which constitutes or is the expression of the surface tension. A blood clot results from the conversion of fibrinogen from a soluble form (hydrosol) into fibrin—an insoluble state (hydrogel). This process of contraction of gels with the separation of some liquid (which is a saturated solution of the material of one phase of the gel, generally the solid matter containing other substance in solution such as salts) is known as syneresis. When a blood clot contracts due to shortening of fibrin particles, serum is squeezed out; agar-agar and gelatin contract, giving rise to so-called water of condensation; likewise serum contracts, losing its water, and becomes hard. Collodion behaves in this manner also.

Fig. 1.—Healing by first intention (dog). The section was taken after forty-eight hours. The defect was filled with a blood clot, which was lost in making the section. There is less cellular response in the superficial (left) than in the deep portion (mesodermal) of the wound (right)

The body fights with chemical substances (antibodies) and living cells (phagocytes). When an injury occurs, chemical substances (H-substance of Lewis; bacterial toxins, potassium from injured cells, peptones and other split proteins) and nerve reflexes warn the body of its presence. These start the process known as inflammation, which is sustained by an increase in local acidity (caused by relative anoxia, increased percentage of carbonic acid, and concentration of metabolic end products).

Inflammation is chiefly the reaction of mesodermal tissue. Epithelial cells have no phagocytic or other defensive powers and respond to an irritant by degeneration or disintegration as in leucoplakia and hyperkeratosis. But they do have the power of hyperplasia and hypertrophy which may be orderly as seen in repair or disorderly as seen in neoplasia.

PART II

LOCAL RESPONSE AND GENERAL BODY REACTIONS TO INJURY

Chapter 3

REPAIR—THE REACTIONS OF TISSUE TO MECHANICAL TRAUMA

In its broadest sense this entire book is a study of repair. Whether damage is done by mechanical, bacterial, or chemical causes, by neoplasia, or even by normal wear and tear, the process of healing is involved.

In every instance we are not only interested in the cause of the injury but more perhaps in the manner that tissues react to the insult, even in the case of neoplasia.

Living things are different from inanimate objects in many ways. The former have the power of growth, reproduction, the ability to metabolize food for the nourishment of their cells or tissues, and the faculty of repairing any defects which may occur.

Nature usually restores continuity by like or unlike tissue, but she may not always restore function of tissue. *Repair* may be defined as the ability of living matter to restore itself to a sound or good state after injury. There are several methods of repair.

Healing by First Intention, or Repair of Aseptic Closed Wounds.—An incision made with a clean sharp instrument induces a minimum of trauma and represents the ideal wound for healing by first intention. First there is some bleeding. Within about four minutes this blood, which has been pouring out, clots. Fibrinogen, which changes to fibrin, is responsible for clotting of the blood (see Chapter 13). Within three or four hours an exudate begins to form. It comes from the blood vessels and tissues that surround the wound and is composed partly of fluid (blood plasma, serum, and lymph) and partly of cells. Plasma is important because it helps combat infection. The serum is also important because forms a scab or crust when it dries and gets hard—nature's antiseptic and impermeable dressing. Lymph carries larger protein molecules and particulate matter to neighboring nodes and ultimately back to the blood stream.

Protoplasm may be regarded either as a very viscid sol or as a gel. Its structure is that of a microscopic emulsion. It can contract and thus press out a solution or it can take up water. In a porous mass such as porous clay, water is taken up in the previously formed spaces. Plants and animals take up fluid by osmosis through

permeable membranes. A homogeneous, pore-free masslike gelatin and most proteins absorb liquids, undergoing an increase in volume—this is called molecular imbibition (Fick).

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More capillaries open, there is an increase of blood to the part (*active hyperemia*), and cells and plasma are poured forth (exudation). This exudate consists of leucocytes (to fight infection); phagocytes, consisting of macrophages, histiocytes, and other reticulo-endothelial cells (to carry away debris, thus performing nature's débridement); fibroblasts (to produce collagen and ultimately fibrous tissue); and endothelial cells (to form new capillary loops).

Menken showed an increased permeability of the capillaries in inflammation, permitting plasma to escape into the injured area. The exudate is rich in fibrinogen and globulin.

The granular leucocytes (which are formed in the bone marrow from myeloblasts) migrate out of the vessels at the beginning of inflammation and then rapidly degenerate in the tissues. They are capable of engulfing cellular debris and digesting it within their substance due to leucoprotease. The wound contains cellular and other debris which is removed by autolysis (tryspin and pepsinlike enzymes from dying cells) and heterolysis, a function of leucocytes which also liberates leucoprotease which acts like trypsin and erepsin. Their action is inhibited by antienzyme of blood serum.

Phagocytes, also called mononuclear exudate cells, or polyblasts are said to arise from endothelium, macophages, blood lymphocytes, or monocytes. Polyblasts also arise from histiocytes. They are mononuclear and nongranular. Their function includes ameboid movement and phagocytic action and they are capable of becoming fibroblasts. Together with the fibroblasts they migrate along the fibrin filaments due to differences in electrical potentials (stereotropic response).

Fibroblasts keep their original nature and function; that is, they do not give rise to other cells except fibrocytes. They develop from reticuloendothelial cells, monocytes, macrophages, and endothelial cells. Although fibroblasts play a role in the formation of collagen, the polyblasts are probably chiefly concerned in the formation of this material. Fibroblasts become fibrocytes in collagen. This substance is derived from precollagen, which appears about the fifth day and takes the silver stain. It is immature and has little cohesive power. On the tenth to twelfth day collagen appears. It does not take the silver stain, is mature, and affords strength to the wound.

Many theories exist as to the origin of this substance. Haidenheim believed that connective tissue fibers develop in a peripheral ectoplasm which takes the form of a syncytial spongework. In such a syncytium argyrophilic networks appear as a result of vital metabolism of the syncytium itself. Maximow thought that the connective tissue fibers result from a crystallization of a semifluid, amorphous, secreted substance which occupies the intercellular spaces. Baitsell stated that the fibrin net fuses and consolidates into wavy fibrils which unite to form wavy bundles. The cells are first round, then flat, and then spindle shaped due to pressure of collagen bands. The substance is probably extracellular in origin.

Wound healing, then, is due to fibroplasia which results from resting undifferentiated cells closely related to the mesoblast. The differentiation of the fibroblasts into specific adult tissue is the result of, and occurs in the same manner as, the structures originally changed from embryonic mesoblastic tissue to adult fibrous tissue.

The cells go to work at their respective tasks. The fibrin in the blood clot acts as a scaffold for them to work upon. This period lasts about four to five days and is known as the lag period. The wound is weak and gains no strength during this time. About the fifth or sixth day large numbers of fibroblasts and endothelial cells appear (proliferative phase). Many causes have been suggested for this sudden stimulus. Some of these are

anoxia, embryonic tissue juice from new cells (trephones), protein split products, glutathione, hemoglobin, sulfhydryl group—SH, and wound or intercellular hormone. Perhaps it is not a stimulation of cells, but, as in the case of neoplasia, perhaps it is a controlled release of the inhibition which normally keeps fibroblasts from proliferating.

The fibroblasts are sparsely present for about four days and then are suddenly seen in large numbers. Their function is to form collagen, a soft gelatinous substance. It is reddish-yellow in color and becomes more red as new capillaries form and fill with blood.

Endothelial cells come from the ends of cut capillaries. They have motility and digestive powers and invade the fibrin mesh. They arrange themselves in parallel rows and unite the capillaries of the two sides and then become canalized, forming new capillary loops. This canalization is due to clot retraction, hydrostatic pressure, and collateral formation.

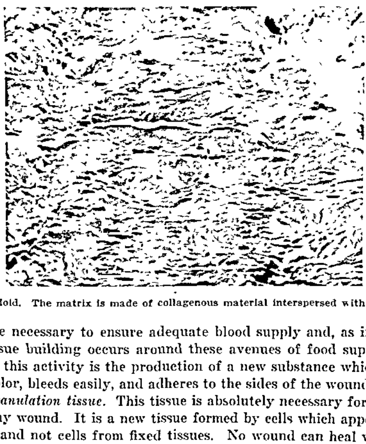

Fig. 2.—Keloid. The matrix is made of collagenous material interspersed with fibroblasts.

These are necessary to ensure adequate blood supply and, as in the embryo, tissue building occurs around these avenues of food supply. The result of this activity is the production of a new substance which is soft, red in color, bleeds easily, and adheres to the sides of the wound. This is called *granulation tissue*. This tissue is absolutely necessary for the healing of any wound. It is a new tissue formed by cells which appear in the exudate and not cells from fixed tissues. No wound can heal without it and having fulfilled its purpose it changes to scar tissue. If there is too much granulation tissue around the wound, the laity call it "proud flesh." Excessive scar tissue (keloid) is really a fibroma and exists not only in epithelial but in other tissues as well. For example, Dupuytren's contracture of the palmar fascia is probably due to a keloid of this substance.

With granulation tissue filling the wound, the epithelial cells begin their work under the protective crust of serum that has formed over it. *The epithelial cells on either side of the wound grow across and cover the granulation tissue (epithelialization).*

Epithelial cells show some ameboid movement. The cells get their stimulation from adjacent cells. At first there is only one layer—stratum germinativum. *In skin grafting this is the layer that is most commonly transplanted* and depended upon, although the whole skin may also be used. The stratum granulosum and lucidum could possibly grow due to plasma from granulation tissue. Epithelialization begins after a latent period of three to six days. Frequent dressings or antiseptics may prolong this by tearing away or devitalizing the advancing cells. Howes stated that the average *rate of epithelialization over recently formed granulations is 1.5 mm. daily*. The rate is not influenced by the size of the wound, nor is there a greater rate after the start than at ten days. There is no particular rhythm or rate; sudden "bursts" of activity occur. Local conditions may slow it and infection stops epithelialization entirely. Microscopically it is characterized by (1) hypertrophy of uninjured epithelial cells at the edge of the wound; (2) the migration of these cells outward over a suitable granulating base; (3) mitotic division; and (4) restratification, which will be slower where the skin is thick (palms and soles). Tropism is not seen.

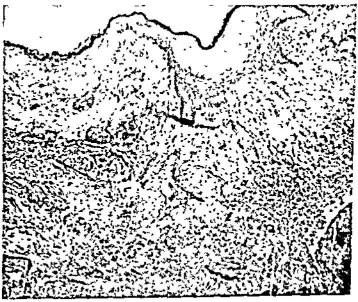

Fig. 3.—Healing by first intention (dog). *Fourteenth day* Epithelialization is complete. There is a minimum of scar tissue. Experiments have shown that a pure culture of staphylococcus, rubbed on an operative wound in an experimental animal after the first day, will almost invariably be followed by an *infection leading to septicemia* and often death of the animal. If this same procedure is repeated after the development of local immunity, which occurs about the eighth day in aseptic wounds, and about the eighth to tenth day in those that are primarily infected, *no local or systemic reactions* occur. Surgeons apply this fundamental principle in everyday practice by not molesting or disturbing the wound for about eight days They also depend upon this phenomenon in removing stitches. The aseptic technique formerly used in *this procedure is unnecessary if trauma is not inflicted.*

After four or five days the wound is filled with fibroblasts and little gray collagen fibers appear. The collagen soon begins to shrink and gets harder. *The strength of the wound increases daily:* healing is about one-third complete on the sixth day, two-thirds by the eighth day, and almost complete by the fourteenth day. Scar tissue forms from collagen, and

as it contracts it squeezes the newly formed capillaries which have made the wound appear red; in about six months they are completely occluded, making the scar white. This is known as healing by first intention, or healing with a minimum amount of granulation tissue.

Scar tissue is, in reality, a substitute for injured or destroyed tissues. Lacking tone, it often stretches under tension. Surgeons should follow natural creases or wrinkles and should know the direction of elastic fibers in the skin so that incisions may be made parallel with them, thereby avoiding wide scars.

The skin is composed of ridges and sulci. From the latter emerge the hairs. Esricht of Denmark first plotted the hair lines in 1837. Later Langer plotted skin tension lines by making small holes in the cadaver and examining the separation of their edges. Kocher later made tiny incisions and checked their separation. These followed the direction of the connective tissue strands in the dermis and the hairs in the epidermis.

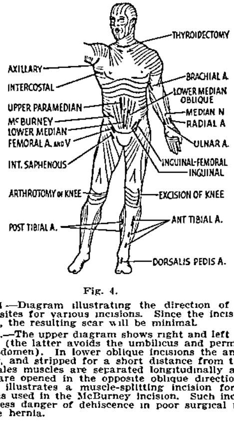

Fig. 4.

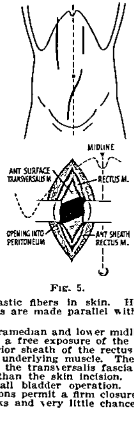

Fig. 5.

Fig. 4.—Diagram illustrating the direction of elastic fibers in skin. Heavy lines indicate sites for various incisions. Since the incisions are made parallel with the elastic fibers, the resulting scar will be minimal.

Fig. 5.—The upper diagram shows right and left paramedian and lower midline oblique incisions (the latter avoids the umbilicus and permits a free exposure of the pelvis and lower abdomen). In lower oblique incisions the anterior sheath of the rectus is divided obliquely, and stripped for a short distance from the underlying muscle. The recti and pyramidales muscles are separated longitudinally and the transversalis fascia and peritoneum are opened in the opposite oblique direction than the skin incision. The lower diagram illustrates a muscle-splitting incision for gall bladder operation. The same method is used in the McBurney incision. Such incisions permit a firm closure, with infinitely less danger of dehiscence in poor surgical risks and very little chance for postoperative hernia.

This same principle applies to abdominal incisions for surgical procedures. They are made parallel with the muscle or fascia rather than across it. However, transverse incisions in the upper abdomen cutting across the rectus abdominis are useful and strong, because the transversalis aponeurosis is cut in the direction of its fibers and the rectus sheath is easily approximated. The nerve supply must not be interfered with. This also is a factor in planning incision, especially about the face.

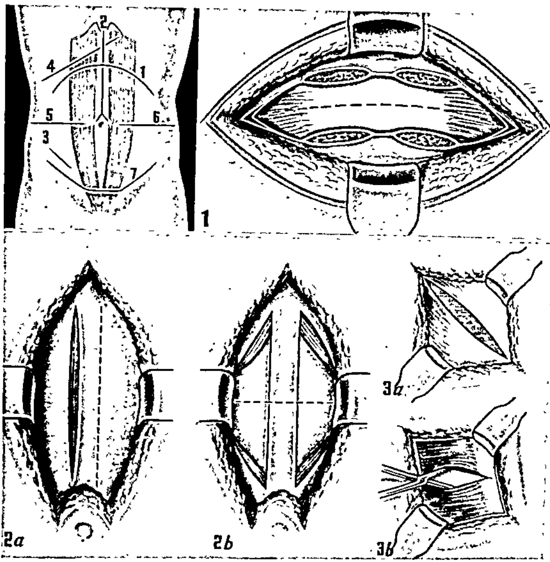

Fig. 6.—The upper left diagram illustrates various sites for abdominal incisions.

1. Transverse incision. This is useful in operations on the stomach, transverse colon, common bile duct, and pancreas. The inverted U-shaped line roughly follows the costal margins. This incision provides for a strong closure and is especially useful in "lateral type" persons whose transversalis fascia fibers run almost horizontally.

Upper right shows the anterior sheaths and both recti divided. The obliques have also been cut on each side. The transversalis is then divided transversely in lateral types or in an inverted U manner in linear types.

2. Midline incision. Many surgeons prefer a right or left paramedian cut so that a cuff of the anterior rectus sheath is left mesially. The incision affords access to the entire upper abdomen, and when it is made slightly paramedian and slanting lateral to the left, the lower esophagus may also be brought into view. When slanted to the left or right into the eighth interspace, a combined thoracoabdominal exposure results. The diaphragm is divided, and on the left side such operations as total gastrectomy, lower esophagectomy, splenectomy and nephrectomy in difficult cases are greatly simplified. On the right, the pancreas and portal vein are easily exposed, facilitating such operations as resection of head of pancreas, portacaval anastomosis, and liver resections. Closure of the transversalis fascia is not difficult because in "linear type" persons the fibers run more obliquely downward than transversely. The right paramedian incisions are used for stomach, pancreas, gall bladder, right colon, and liver operations. *2a* shows a more anatomical incision than the upper midline or the right or left oblique paramedian. The Sloan incision, as it is called, divides the anterior sheath of the rectus on each side of the midline. The recti are retracted laterally and then the transversalis fascia is cut transversely or in the direction of its fibers as shown in *2b.* Sloan found that in longitudinal incisions, the longer the cut, the more force was required to bring the ends of the divided aponeuroses together. The lateral pull on the suture line is in proportion to the square of the length of the incision. When relaxation is not complete, the lateral abdominal tension is about thirty times as great in the vertical as that on the

(Continued on opposite page)

The scar contracts equally in all directions and the final result is a fine white line, like normal skin except for the absence of hair follicles, sebaceous glands, and sweat glands. This is known as *cicatrization* and the scar is called the *cicatrix*.

Healing by Second Intention.—The wound healing by second intention takes exactly the same course as that healing by first intention with one exception—it requires a greater amount of granulation tissue.

If, for any reason, a wound is delayed in its healing, it does not heal "straight across" but heals from the "bottom up." These terms are really misnomers because all wounds must heal in all parts to obtain complete union. It is better to say that more than a minimum amount of granulation tissue is needed to secure repair. The process is exactly the same but a larger area must be filled in with something that will reestablish continuity. This is granulation tissue. For example, the most common cause of *healing by second intention is infection. As we shall* learn later, bacteria destroy cells, leaving large defects in the tissues. Repair cannot be completed as long as the infection continues because the bacterial toxins will destroy all attempts at repair. The process of repair is the same as in the healing by first intention; however, a larger number of polymorphonuclear leucocytes and macrophages will be found among the cells in the exudate. We have seen that inflammation is necessary to obtain repair of tissue, but repair will not occur unless a *local immunity* is established which annihilates the bacteria, or, more correctly, creates an environment unfavorable for bacterial growth, permitting the local immunological agents to destroy the invading organisms. Thus inflammation and repair are not synonymous, and inflammation and immunity are not the same. Inflammation may occur without repair but the reverse is not true, and in order to secure repair in an infected wound it is necessary to have inflammation and immunity.

Repair begins shortly after injury. It differs from bacterial inflammation in its immunological qualities and its anatomical appearance. A pyogenic membrane is produced by the exudates of inflammation, aided by the forces of repair and immunity,

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suture line of the transverse incision. (Sloan, G. A.. A New Upper Abdominal Incision, Surg., Gynec. & Obst. 45: 678, 1927. 2b. Incision through the transversalis fascia.

3. *McBurney incision. An anatomical incision usually employed in operations on the* appendix or cecum. 3a. The external oblique fascia is divided in the direction of its fibers. 3b. The internal oblique and transversalis muscles are split in the direction of their respective fibers, then the peritoneum is opened obliquely parallel with the skin incision or transversely.

4. Subcostal incision. Used in gall bladder and bile duct operations.

5. Right-sided transverse incision. Used for approach to the ascending colon and cecum; also in right lumbar sympathectomy (extraperitoneal). The incision in the last instance is muscle splitting, that is, the transversalis sheath is incised and the rectus muscle pulled medially, and then the obliques and transversalis muscles are split in the direction of their fibers.

6. Left-sided transverse incisions are useful in operations on the descending colon and spleen and in left lumbar sympathectomy.

7. Low transverse incision (Bardenheuer). All of the layers of the abdominal wall are cut transversely. Pelvic surgery of all types may be done through this incision. The central and left components of this incision are used in abdomino-perineal resection of the rectum and anterior resections of the sigmoid. The Pfannenstiel incision cuts only the skin and fascia transversely.

and serves to limit infection. It may be looked upon as a special type of granulation tissue (Chapter 4). When bacteria can no longer invade and destroy it, the wound becomes filled with it, permitting repair.

The entire process has been compared by MacCallum to a burning house.

The fire is destroying the house very rapidly. The alarm is sounded (chemical and nerve reflexes), firemen appear (leucocytes) and attach many lines of fire hose (new capillaries and endothelial cells) which bring water (blood cells and plasma), and

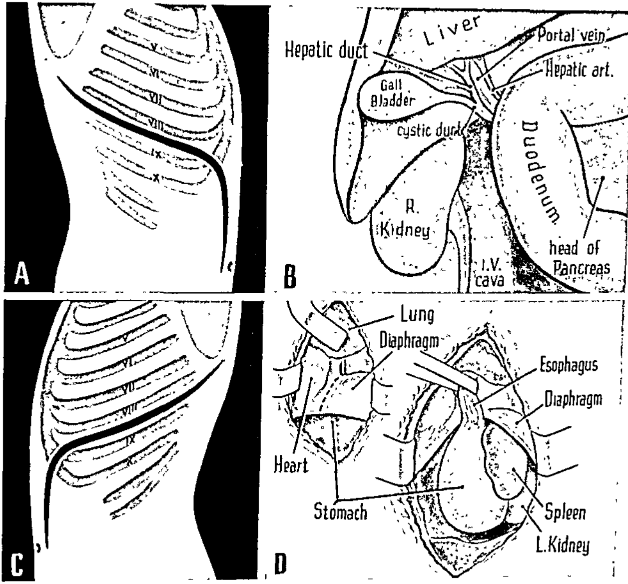

Fig. 7.—Thoracoabdominal incisions. *A.* Right Thoracoabdominal exposure. *B.* This permits easy access to the entire upper right quadrant and is particularly useful in such operations as hepatic lobectomy, repair of stricture or repair of destruction of the biliary duct system, excision of liver neoplasms, portacaval shunts, and pancreatectomy. *C,* Left Thoracoabdominal exposure. *D.* This is extremely useful in surgery of the esophagus, cardiac end of the stomach, spleen, left kidney and adrenal gland, and tail of the pancreas.

Recently we have been using an incision which is a combination transverse and thoracoabdominal with excellent results. It is made in the direction of the eighth interspace and carried upward.

chemicals (antibodies). Carpenters start the process of reconstruction (fibroblasts). Of course, if the fire breaks out anew, the new material will be destroyed again (destruction of granulation tissue); but if it is extinguished, *their efforts will ultimately reconstruct the dwelling*. It will not be perfect in material or contour (absence of hair follicles, sebaceous, and sweat glands; or cicatricial contraction) but will be serviceable and not too unsightly if the destruction is not too widespread. In the latter event a portion of the house may have to be rebuilt (surgical aid—skin graft—may be needed to prevent undue distortion).

Granulation tissue is insensitive at first because nerve fibers have not grown into it. This process begins in six to twelve weeks. After the wound has filled with granulation tissue, a little thin gray membrane creeps across the top; this is the new skin (epithelial cells which are really the first layer of the stratum germinativum). Finally it grows across and the wound is healed. Later the epithelium becomes stratified in the skin and mucous membranes. The connective tissue within the wounds forms the *scar or cicatrix, which contracts equally in all directions* (length, width, and depth). This structure is weak and may stretch

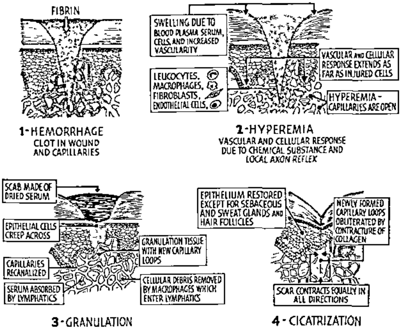

Fig 8.—Diagram indicating stages in wound healing. It must be understood that these events do not occur chronologically, as independent stages, but that they overlap; however, it may be said that by the fourth day fibroplasia has begun, and by the end of two weeks healing is normally complete.

1. Immediately after an incised wound is made there is bleeding. Clotting occurs due to fibrin.

2. The tissues react to the injury by increasing the blood supply to the part (hyperemia) and by the attraction of cells. This response may be due to chemotactic or nervous influence or to a local, axonal reflex dilatation of the capillaries. Cells are shown in the lumina of the capillaries and around them.

3. Stage of granulation. Capillaries are recanalized and have grown across into the granulation tissue, making it red. Plasma and serum are absorbed by the lymphatics. Epithelium is creeping across the granulation tissue under the protection of the scab which hardens due to syneresis. The epithelium is at first one cell-layer thick, and this is the stratum germinativum. From these cells the other layers develop in stratified squamous epithelium. The stratum corneum may take a long time to form in such thick skin areas as the soles of the feet and the palms of the hands.

4. Cicatrization. Contraction occurs in length, width, and depth.

and serves to limit infection. It may be looked upon as a special type of granulation tissue (Chapter 4). When bacteria can no longer invade and destroy it, the wound becomes filled with it, permitting repair.

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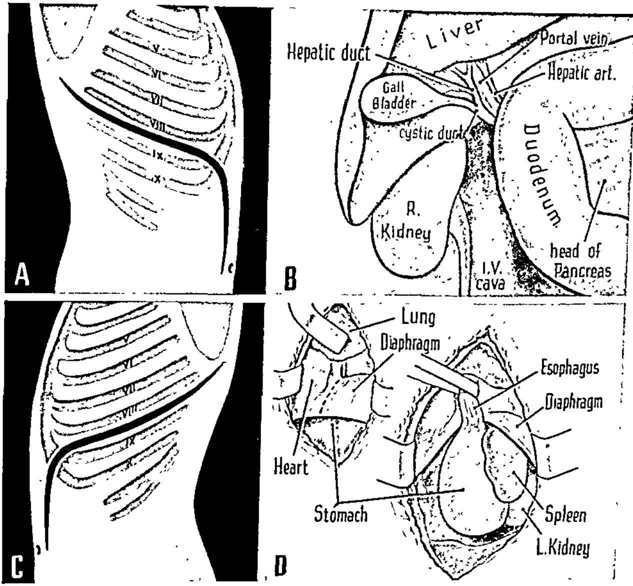

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processes or changes in hydrostatic or osmotic pressures. The latter includes cells and plasma which migrate through dilated and more permeable capillaries. It is apparent that the former will contain less protein because this molecule is too large to traverse the normal capillary wall. It is the distention of tissue spaces with the fluid preventing proper blood supply and tissue cell migration rather than the characteristic of the transudate which delays healing.

Epithelization sometimes occurs before granulation tissue fills the gap. This leaves a *dead space* which fills with serum or exudate. It will open again, for healing must be from the bottom up.

Healing by Third Intention.—Healing by third intention was reintroduced during World War I. In this case the surgeon brings together by suture or butterfly of adhesive tape two walls covered with healthy granulation tissue. (The fact that local immunity has been established must be shown by a minimum amount of pus and active proliferation of granulation tissue.) By this method much time can be saved in the healing process, through probably, immobilization of the wound's edges and a reduction of its size.

FACTORS WHICH INFLUENCE THE HEALING OF A WOUND

1. Infection
2. Size of the wound
3. Blood supply (passive congestion and anemia)
4. Rest
5. Foreign bodies
6. General condition of the patient
7. Miscellaneous causes

Infection.—*All wounds are contaminated.* This means the presence of bacteria at the site of injury; but *the mere presence of bacteria does not constitute infection.* If the wound is properly cared for within six to eight hours, infection may not occur. Infection delays healing until immunity occurs and the infection is annihilated. The healing takes place by second intention. If the infection is not overcome, healing will not take place, granulations will become fibrosed (cicatrization), and chronic ulcers will form. Surgeons guard against infection in surgery by using an "aseptic" technique and in contaminated wounds by thorough cleansing (see Chapter 16).

The technique of modern surgery is nearly aseptic. In spite of the most rigid cleansing and disinfection of the abdominal wall, some residual bacteria remain in the hair follicles and sebaceous gland ducts, although the "transient" flora of bacteria have been removed. Furthermore, due to bacteria in the air of the operating room and those which escape careful masking of the surgeon's face, a surgical wound contains more bacteria at the conclusion of an operation than at its beginning. In addition, the surgeon's hands, although carefully scrubbed and disinfected with 70 per cent alcohol (supposedly the most efficient disinfectant for this purpose), will show more bacteria after gloves have been worn for the dura-

subsequently under pressure. In the abdomen this may give rise to hernia. It is important to emphasize the fact that *the greater the delay in healing, the more granulation tissue; and the more of this, the greater the scar and the subsequent contracture;* the more trauma or injury, the greater the delay. Surgeons therefore, handle tissue gently and carefully, because they know that *healing occurs in inverse ratio to the degree of trauma.*

An incision for the performance of a surgical operation should be made as close to the site of the disease as possible. This minimizes trauma.

A. B.

Fig. 9.—Healing by second intention. *A.* Rabbit's tongue. No suture used. The mucous membrane dips down into the wound. There is a wide scar. *B.* Edge of burn. Granulation tissue has filled the defect.

Any factor which increases the exudative reaction beyond normal causes a delay in healing. This delay may be due to local factors such as infection, mechanical or chemical trauma (strong antiseptics, local use of sulfonamides, talcum powder, etc.), foreign bodies (dead tissue, blood clot, large amounts of suture material, especially catgut, and, in the presence of infection, nonabsorbable sutures perpetuate the delay until extruded), and extremes in temperature, whether cold or hot. The general factors causing an increase in exudation include low osmotic pressure of the blood due to hypoproteinemia or hydremia, which may be due to hyperhydration; dehydration with stagnant anoxemia and leaky capillaries; anoxemia; general debility as seen in advanced carcinoma (cachexia) which is really a combination of many factors, q.v.; also allergy to catgut has been suggested by experimental and chemical reports. Thus we see that transudates as well as exudates may delay healing. The former may be looked upon as the fluid part of the blood leaving normal capillaries because of normal physiological

healthy granulation tissue. Vascularization takes place through the capillary loops in this tissue. Some or all of the stratum germinativum is taken, and from this, as in normal repair, restratification occurs. Undoubtedly, transplanted cells from the stratum granulosum and even lucidum may survive. The more common types of free grafts are: Reverdin (pinch), which are usually placed on the surface but may be buried in the granulation tissue; Ollier-Thiersch, or the thin split graft; thick split graft and Wolfe-Krause, which is a full thickness of the *skin* containing dermal elements as well. The split graft may be used on most raw surfaces and has the advantage of leaving part of the stratum germinativum on the donor *site*, thereby avoiding its grafting.

FIG. 11.—Extensive burn covered with infected crusts. These must be removed so that healthy granulation tissue may form. The area is then covered with Thiersch or split-thickness grafts.

An ingenious method of maintaining the position and contact of a free graft has been devised by Sano. He employs the patient's own blood, using the buffy coat (white cells) after centrifuging. These cells are mixed with Tyrode's solution (a buffered salt solution) and the cell mixture or extract is applied to the undersurface of the graft. Large split-thickness grafts are usually immobilized by silk sutures; then immobilization of the part is secured by casts or splints and pressure bandage.

When large deep areas must be built up, *pedicle* grafts are used. A flap of skin may be used or simply *transplanted by parallel or Z incisions, leaving its end or ends*

tion of the average operation. These considerations have led to "soap and water" cleansing of the abdominal wound before closure, ultraviolet radiation of the surgical room, more efficient face masks, change of gloves and "second scrubbings" in the longer operations, etc., as we shall see in Chapter 5. Ultimately the development or nondevelopment of infection depends on the resistance of the patient's tissue cells. *If local immunity* is normal, a minimal number of contaminating organisms will be harmless. If devitalization occurs due to extensive trauma, the devitalized tissue wherever possible should be excised. Still more desirable is atraumatic *surgery*.

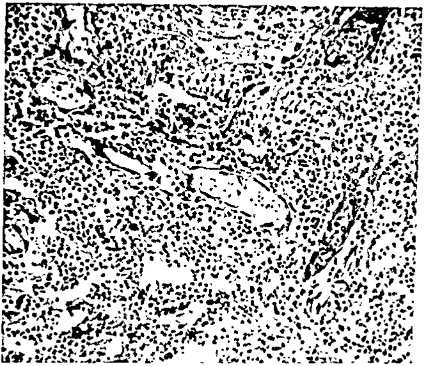

Fig. 10.—Granulation tissue from an infected wound. There are many capillary loops. Fibroblasts, polymorphonuclear leucocytes, lymphocytes, and macrophage cells are present in large numbers.

Size of Wound.—In large burned areas, for example, in which infection has been overcome, healing is also delayed. The epithelium can grow only across a certain distance, which is variable but for unknown reasons limited. Some believe this is due to lack of chemotactic influence. As scar tissue contracts, the size of a wound becomes smaller, permitting epithelialization to occur. *As uncovered granulation tissue* grows older, it contracts, obliterating the newly formed capillaries and ending in a pale, fibrosed bloodless mass of tissue which does not fill in the defect. This is the formation of what is known as an *ulcer or sore.* After extensive burns, skin grafting is done on the healthy granulation tissue as soon as it fills the wound, thereby preventing vicious scars or ulceration and hastening healing.

There are many ways of transplanting skin from one part of the body to another (autogenous). Although sporadic reports of *successful isogenous, homogenous, and* even heterogenous skin grafts appear, we have been unable to duplicate these feats. *Free* grafts imply the complete separation of the donor skin and its transplantation on

healthy granulation tissue. Vascularization takes place through the capillary loops in this tissue. Some or all of the stratum germinativum is taken, and from this, as in normal repair, restratification occurs. Undoubtedly, transplanted cells from the stratum granulosum and even lucidum may survive. The more common types of free grafts are: Reverdin (pinch), which are usually placed on the surface but may be buried in the granulation tissue; Ollier-Thiersch, or the thin split graft; thick split graft and Wolfe-Krause, which is a full thickness of the *skin* containing dermal elements as well. The split graft may be used on most raw surfaces and has the advantage of leaving part of the stratum germinativum on the donor site, thereby avoiding its grafting.

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When large deep areas must be built up, *pedicle* grafts are used. A flap of skin may be used or simply transplanted by parallel or Z incisions, leaving its end or ends

attached. Tube grafts are rolled flaps of skin which are "waltzed," "jumped," or "caterpillared" into position by successive planned implantations leading to the final destination. Inlay grafts (Essen) are split-skin grafts on molds which are buried raw side out in the tissues and then later opened and transplanted to conform to a cavity about the eye or mouth. Tunnel grafts are whole-thickness transplants beneath the skin.

Combination grafts are also known as delayed pedicle grafts. Here the blood supply is poor and the pedicle of skin is elevated and then returned to its former position so that its blood supply will be increased and granulation tissue may form on its undersurface. Such grafts may be lined with thick split grafts and used to reconstruct the cheek, nose, etc.

Fig. 12.—Vicious cicatrix due to a burn. The deformity was corrected by forming a tube graft (jump, waltz, or caterpillar) on the abdomen and "waltzing" it into position. Then when ready to sew down, the scar was excised and the graft opened and sutured into the excised area.

Other tissues may also be freely transplanted. These are mucous membrane, fascia, tendon, cartilage, and bone. Fat is used as a free transplant but is perhaps more successful if on a pedicle. A whole muscle not deprived of its blood supply is frequently transplanted in orthopedic surgery; also in chest surgery to fill in large empyema cavities. Homogenous grafts of cartilage, corneal tissue, bone, and even organs such as veins and arteries have been successfully used.

Epithelial *grafts send out cells which join the grafts to each other* and to the wound margin. Thus it will be seen that the size of the wound may delay healing even if there is no infection; and the more the delay, the more granulation tissue; the more granulation *tissue, the greater* the scar; and the more scar, the more contraction. When vicious con-

tractures occur, the surgeon must start from the beginning, remove the scar surgically, and then perform a skin graft or a tube graft operation.

Blood Supply.—Tissues must have an adequate blood supply in order to heal. Anemia of tissue may not only delay healing, but cause sloughing as well. Sloughing is often caused by plaster casts applied too tight and allowed to remain on for long periods without careful inspection.

Fig 13.—Thiersch grafts in place. Note the free movement of the arms.

Wounds may break open because sutures were put in too tight by the surgeon. Sutures should be tied loosely and a wound should never be sutured under tension It is far better to make skin flaps or leave the area for subsequent skin grafting. The same principle holds in all tissues and organs. If there is a poor blood supply due to arterial disease, such as arteriosclerosis or thromboangiitis obliterans, the wound will be very slow to heal. It is important to test the blood supply of the extremities in the aged and those afflicted with diabetes before during operations on the feet.

Therefore, when a patient with arterial disease develops gangrene, necessitating the amputation of a lower extremity, the surgeon should amputate at the thigh if necessary, where the blood supply is adequate for good wound healing (see Chapter 6).

Blood stasis delays healing. A wound in the lower tibial region is very slow to heal. Standing produces a certain amount of passive congestion in the legs. Waste products cannot get away; fresh blood cannot get in. This is *stasis with resulting asphyxia of tissue, and it not* only prevents healing, but in certain conditions causes devitalization as well. Patients with varicose veins have much more stasis than normal individuals, for no valves are present in these veins. Such patients usually come to the surgeon with a history of a small scratch which will not heal. An elastic bandage should be applied in all cases of leg wounds,

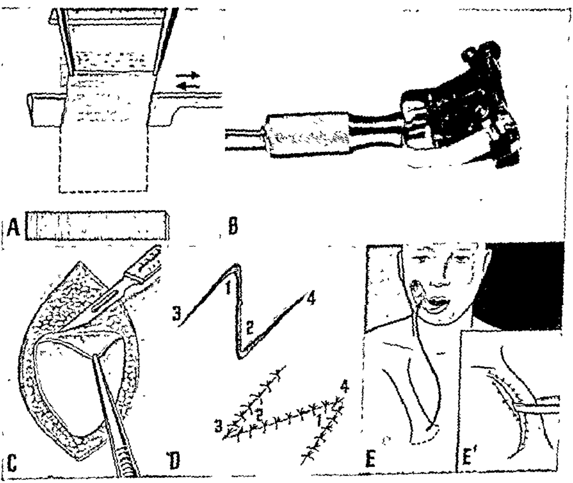
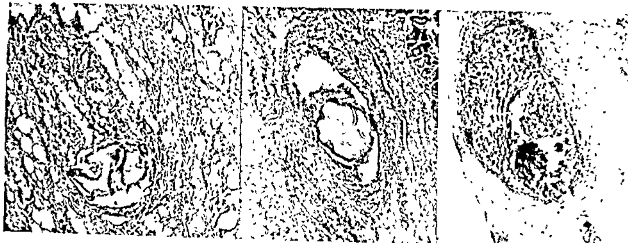


Fig. 14.—Diagram illustrating various methods of skin grafting and Z-plasty. *A.* Split-thickness graft. *B* The Brown electro-dermatome *C. Reverdin graft. D. Z-plasty.* A useful procedure in the treatment of contractures due to vicious cicatrization. Although the illustration shows only one Z, the operation may be extended to two or more Z maneuvers. *E* and *E'* *Pedicle graft.* The plan of a pedicle is based upon the preservation of an adequate blood supply in the two attached ends, if the graft is fashioned in line with a blood vessel such as the superficial epigastric, the distal end may be detached and sewn into place as, for example, on the dorsum of the hand in one operation. Otherwise such grafts are moved after the blood supply has become established. One side is detached at a time so that the pedicles will be maintained during the "waltzing" maneuvers.



A. B. C.

Fig. 15—*Different types of suture material after ten days (dog).* A. Plain catgut There has been almost complete disintegration of the catgut. The tissue reaction is pronounced B. Chromic catgut No. 0 The suture is intact There is less reaction than in A. C Silk The strands of silk are slightly separated by serum. There is almost no tissue reaction. The same is true of cotton suture. Linen remains intact better than silk and causes even less reaction

even in normal individuals, thereby limiting stasis, so that normal repair of wounds may occur. It should be emphasized, however, that pressure should never be applied to such a degree that there results an interference with the blood supply. If this is done, the viability of tissues is endangered and within a variable period (twelve to seventeen hours) massive necrosis may occur.

Rest.—Needless to say, a wound cannot heal with a minimum amount of granulation tissue when the edges are in motion. A dog with a wound lies quietly in the sun and licks the raw surface. (Rest and cleanliness?) When a surgeon sutures a wound or puts a broken leg in a cast, he puts the two divided edges at rest. Rest to the part is necessary for healing, so that there will be a minimum of granulation tissue.

Wounds are sutured to obtain rest and immobilization, reduce trauma to their edges, and decrease the size of the gap until repair is complete. Various materials are available for wound coaptation. In general, it may be said that if the divided tissues can be held in apposition without the aid of sutures, this is desirable; for example, adhesive on the skin, a plaster cast, or splint for fractures. Two factors are important in selecting a suture—the type tissue involved and its condition (infected, contaminated, badly contused, or normal) and the qualities of the suture material (strength, reaction engendered, absorbability, ease of handling, sterilizing, and cost).

Two general types of sutures are used: absorbable (plain and chromic catgut, kangaroo tendon, fascia) and nonabsorbable (cotton, silk, linen, rayon, cellophane, and metals such as silver on tantalum wire, pins, and clips).

Even in normal tissues their structure is important in selecting a method of securing rest. For example, bone is not successfully held by sutures and, moreover, porous bone may require a large piece of metal. The ideal suture is one which will remain intact long enough to secure rest to the divided structures and which will cause a minimal reaction in the tissues. For this purpose in clean wounds cotton, silk, or linen may be used. For infected, badly contaminated or contused wounds, sutures are used to control bleeding and not to close the area unless thorough débridement is possible—in such instances catgut is best. Plain catgut causes great reaction and is quickly absorbed. It is therefore not so reliable as chromic catgut. Smaller sizes such as 0 and 00 last as long as, or longer than, larger sizes, for they are more thoroughly impregnated with chromic acid or iodine. Also, a double strand of small catgut engenders less reaction than a single strand of large suture, because it is harder for the tissue wandering cells to attack the former. In general, the more inert the material used, the less the reaction to it, and the less the reaction, the more rapidly healing will take place.

Strength of Suture Material.—Halsted's dictum, that it is not necessary to use a suture stronger than the tissues which are brought together, is true because it will be the tissue that will give under tension. All sutures lose tensile strength after implantation. The strength of chromic catgut is highest before implantation but lowest after ten days. Cotton is said to have the least tensile strength before and the most after ten days. Silk is weaker than catgut but stronger than cotton before and weaker than cotton after ten days in the tissues. There is little difference in the tensile strength between plain and chromic catgut.

Other Considerations.—Microorganisms are said to be found much more commonly (five times) in catgut sutured wounds than in silk sutured wounds. This is probably due to the irritation of the former permitting indigenous bacteria to grow. The lag period is longer in the former (catgut) because the suture is destroyed due to an acute inflammation which produces the prolonged "cellular débridement." There is also a delay in the maturation of fibroblasts and production of collagen due to the great

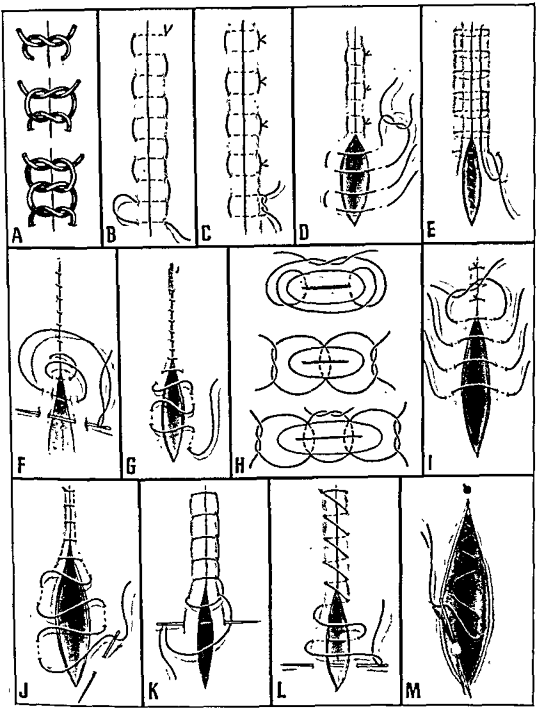


Fig. 16.—Various types of commonly employed stitches and knots. *A.* Single knot, square knot, triple knot. *B.* Continuous mattress. *C.* Interrupted mattress. *D.* Halsted interrupted mattress. *E.* Continuous mattress on-end. *F.* continuous Lembert. *G.* Connell *H.* Ligation of pedicle *I.* Interrupted Lembert. *J.* Cushing. *K.* Blanket. *L.* Over and over. *M.* Subcuticular.

inflammatory reaction. Therefore, *the greater the reaction, the more exudation*, and the more the exudation, the greater the delay in fibroplasia. Some of the tissue reaction to catgut may be due to allergy (q.v.); irritation by the preservatives (xylene, alcohol, solvent naphtha, etc.) large knots required due to low coefficient of friction.

For uninfected wounds cotton or silk is ideal because of the small amount of exudation, ease of sterilization and handling, durability, and high coefficient of friction.

Removal of Sutures.—Skin sutures are almost always nonabsorbable because they do not produce stitch scars for reasons given. Skin sutures are usually removed in clean wounds on the eighth to the tenth day (see legend to Fig. 3). At this time local immunity is high, *and contamination, unless accompanied by gross trauma, will not result in infection.* Also, epithelialization is practically complete and scabs are ready to fall off. If sutures are removed too soon there may be separation of the skin edges and an infection may result. If left too long, some of the suture material (especially black silk *may become infiltrated with scar tissue and may be left in the wound as a* dark streak. Also, there may be considerable local reaction with resultant scars at the sites of the stitches and even across the wound (stitch scars). In surgery of the face and neck many devices have been used to avoid ugly scars. All of the factors which delay healing are avoided. *In addition, incisions are made in normal folds and held* by subcutaneous sutures of fine silk, or if cutaneous sutures are employed, they are removed early, about the fourth day, and opposition is maintained by a few subcutaneous sutures and by adhesive on the surface.

Foreign Bodies.—Wounds will not heal readily with foreign bodies in them. Drainage tubes are introduced in some cases deliberately to prevent healing for a time. Blood clots and devitalized tissue act as foreign bodies. Glass, dirt, grease, hair, etc., must be removed. Anything between the edges of a wound will delay repair. *Pieces of metal or silk, if sterile, may be enclosed within a wound, but not between its edges.* Silk sutures in sterile wounds, or even steel or other metal (wiring of fractures), may remain in a wound without delaying repair, and although the marrow cavity tolerates foreign bodies poorly, intramedullary pins are used successfully in treating fractures. If a piece of muscle lies between two ends of a broken bone, healing may be delayed. Therefore, the surgeon is careful to avoid foreign bodies to operative wounds, and in accidental injuries he is careful *to remove all extraneous material.*

Recently much has been written about *the dangers of talcum powder in surgery. The effects of this substance* have been studied in operative wounds in the brain, peritoneal cavity, vagina, rectum, and other tissues. The reaction is that induced by any sterile foreign body except that it is more vigorous due to its silicate nature because the body cannot readily repair the defects it induces. There is a tubercle-like formation around the granules which is ultimately replaced by fibrosis *and resultant scar. Vicious cicatrices may form, causing ugly scars or* dense adhesions in the peritoneal cavity. Some observers believe that silicosis may result. This is probably not true because little, if any, absorption occurs. Potassium bitartrate is now used in many hospitals, as first suggested by Selig, or starch mixtures may be employed.

General Condition of the Patient.— Dehydration (*due to vomiting,* diarrhea, or lack of fluids) or starvation (*with low blood protein and re-*

sultant edema) may delay healing. Formerly it was customary to starve patients three days before operation. This is not done now. Profound anemia, diabetes, or long debilitating disease adversely affects repair. Modern surgery demands thorough preoperative preparation for this reason. Attention is given to fluid and electrolyte balance (salt solution), nutrition (glucose), and plasma protein (blood and plasma transfusions) in this preparation. In addition, the necesssary vitamins are supplied.

Vitamin A deficiency may result in xerophthalmia. One of the first symptoms is nyctalopia, or night blindness. Minor disturbances of the skin (hyperkeratosis), decrease in general body resistance to infections, and retardation of body growth are also said to result from various amounts of depletions of this vitamin. The effect on mesodermal structures is not clear. Recent experiments on vitamin A-deficient animals show a delay in healing. The local application of cod liver oil apparently accelerates healing in these animals, but there is no proof that this is due to its vitamin A content. There is no evidence that the ingestion of vitamin A prevents the formation of renal calculi in man or that it is useful in the treatment of hyperthyroidism, anemia, nervous disorders, or ulcerations of the skin. The daily requirement is about 5,000 to 6,000 units.

Vitamin B complex is composed of the following substances: (1) thiamine (vitamin B_1, antineuritic antiberiberi factor); (2) riboflavin (vitamin B_2, vitamin G, a growth factor; (3) niacin (nicotinic acid or nicotinic acid amide, P.P. or pellagra preventive factor); (4) pyridoxine (vitamin B6, antidermatitis factor); (5) pantothenic acid (filtrate factor); (6) biotin (vitamin H, coenzyme R, anti eggwhite injury factor, needed for growth of yeasts, molds, and bacteria); (7) paraminobenzoic acid (antisulfonamide factor); (8) inositol; (9) choline; (10) folic acid.

Of these factors, thiamine and nicotinic acid are most important in surgery. The former is useful because its reduction causes an interference with glycogen storage and resultant hyperglycemia. Since it acts as a coenzyme in facilitating the oxidation of pyruvic acid in the body, an increase in the latter has been used as an indication of thiamine deficiency. It is especially indicated before and after thyroid surgery cardiovascular and nutritional effects, gastrointestinal surgery (intestinal effects), and biliary tract or liver surgery (diminished hepatic function causes a decreased ability of the liver to phosphorylate vitamin B for utilization by the tissue). Daily requirement is 1 to 2 mg. or 300 to 600 units.

Nicotinic acid is used before and after gastrointestinal surgery and especially where fistulas of the small bowel must be corrected. Pellagra may occur due to an inability to absorb the nicotinic acid factor or due to its loss through a fistulous opening before absorption can take place. Also, in all obstructive lesions (esophagus, stomach, upper intestinal canal) where parenteral feeding is necessary and in severe diarrhea (chonic ulcerative colitis) this factor must be used. The daily requirement is 20 to 30 mg. in normal adults. None of the B factors should be given alone over long periods because any of them given in large dosage will step up the metabolism of the others which, if not also supplied, will result in a deficiency. Thiamine chloride in large dosage is a method of producing vitamin B deficiency in experimental animals.

Vitamin C, ascorbic acid, also known as cevitamic acid, is the antiscorbutic vitamin. There is no proof that its deficiency causes dental caries, pyorrhea, or gum infections or predisposes to anemia, undernutrition, or infection. Its deficiency does interfere with wound healing because precollagen, devoid of holding power, may be laid low down instead of collagen. The production and maintenance of the intercellular cement substance may be impaired. Bleeding tendencies are said to be due in part to the deficient intercellular structure of blood vessels. It is well to emphasize that deficiency symptoms as just described do not occur until five months on a vitamin C-free diet. Wounds heal normally in subjects on a scorbutic diet for six months. However,

in chronic gastrointestinal disease, where intake is inadequate, or in patients with intestinal fistulas or chronic diarrhea, ascorbic acid should be given pre- and postoperatively. The daily requirement in normal persons is 75 to 100 mg.

Vitamin D probably represents more than one substance. A deficiency may interfere with the proper utilization of calcium and phosphorus, causing rickets, spasmophilia (infantile tetany), and osteomalacia. The vitamin may be important in tooth formation and maintenance and indirectly with blood clotting (calcium metabolism) and the repair of bone.

Calciferol (vitamin D_2) is irradiated ergosterol. Daily requirement for growing children or during bone repair is 400 units.

Vitamin K *is necessary for the synthesis of prothrombin which is formed in the* liver. Its deficiency produces hemorrhagic tendencies due to a hypoprothrombinemia. Vitamin K_1 is manufactured by the green leaf and chlorophyll-containing plant organs (alfalfa, spinach, etc.). It is therefore obtained by the ingestion of such plants. Vitamin K_2 is formed during the course of putrefaction and is formed in man in the large intestine. Vitamin K is therefore available at all times from exogenous or endogenous sources in the normal individual. It is indicated in (1) prolonged dietary deficiencies; (2) obstructive jaundice; (3) primary hepatic disease; (4) hemorrhagic states which exist in chronic intestinal diseases, whether due to loss of continuity (fistula) or absorptive surface (chronic ulcerative colitis, amebic dysentery)—in such instances the patient does not eat vitamin K-containing foods due to anorexia and their laxative-producing quality (exogenous sources) and absorption cannot occur due to destruction of mucous membrane (endogenous sources); (5) physiological hypoprothrombinemia of the newborn; (6) when succinylsulfathiazole (sulfasuxadine) or Sulfathaladine is administered for preoperative preparation in colonic surgery or in the treatment of various types of colitis; here the coliform bacteria are so greatly reduced that K_2 is not available.

The daily *requirement is not definitely known.* When *given by mouth,* bile is necessary for its absorption. Usually it is given intramuscularly; 2-methyl-1,4-naphthaquinone (menadione) is given in 2 to 4 mg. doses daily until the prothrombin time approaches normal.

Vitamin P (citrin) is said to control vascular permeability. It may be a factor in vitamin K.

This discussion does not mean that every surgical patient must have all of the vitamins mentioned. It does mean that in the preparation for surgery and in the aftercare these deficiencies must be corrected if present and anticipated if dietary requirements cannot be met. In succeeding chapters their specific uses *will be stressed; also* the daily water, salt, caloric, and protein requirements will be considered.

Trauma to tissue whether mechanical or through maceration or caused by the use of strong antiseptics (an antiseptic strong enough to be bactericidal may also be fatal to cells), will produce all the obstacles to wound healing previously mentioned. Death of tissue cells decreases local resistance and permits *infection* to occur, cellular debris acts as a *foreign body, the size of the wound* is increased, *blood supply* is interfered with, and the *general condition of the patient* is jeopardized because of absorption of toxic products.

Miscellaneous Causes.—

Temperature.—My associates and I studied wounds in guinea pigs which were observed at various temperatures. Excessive heat or cold delays healing. Brooks and Duncan found that heat hastened and cold delayed the inflammatory *reaction. Wounds heal best* in moderate tem-

peratures. Much has been written lately on the use of cold (cryotherapy) in the treatment of wounds (see Chapters 4, 5, and 6). It is wrong to assume that either heat or cold is indicated as a therapeutic measure in the presence of adequate blood supply. High fever also delays fibroplasia; this may be due to the increased temperature per se or its causes.

Acidosis and Alkalosis.—Wounds normally heal in a medium which is acid in reaction. Acidity favors vasodilation; however, when too acid (pH below 5) or too alkaline (pH above 7) vasoconstriction occurs. Slight acidity is said to favor vasodilatation, exudation, the action of autolytic enzymes, the more complete dissociation of oxygen, and local inhibition of bacterial growth.

Neoplasia.—Wounds made into malignant growths may heal but will do so with malignant cells. The process was studied in experimentally induced sarcoma. There was no localized increase in growths due to the wound healing stimulus which was superimposed on the already present proliferative stimuli within the malignant cells. There was no ingrowth of nonneoplastic tissue from the immediate vicinity about the sarcoma.

Diet.—Complete starvation does not alter the healing of a wound, although the lag period may be prolonged. After operation on the gastrointestinal tract, it is more important to attend to water balance and osmotic pressures than to food. The vitamins should be administered, especially thiamine chloride, ascorbic acid, and nicotinic acid. The velocity of fibroplasia and its proliferation is enhanced by high protein diets. Hypoproteinemia delays wound healing by decreasing osmotic pressure and permitting edema to occur. If this is corrected with acacia in the experimental animal, healing is normal. A general poor state of nutrition is more important in wound disruption than is hypoproteinemia. Carbohydrates are necessary also to secure good repair. Fat prolongs healing.

Age.—The lag period is longer in the aged, but once fibroplasia begins there is no difference. This means that the tensile strength of a wound after surgery is weak for a longer period of time. Wounds seem to heal faster in the young, and it has been said that the rate of healing is inversely proportional to the age. Surgery is often done on older persons and they must be mobilized early to prevent complications. Since the terms old and young are used in a relative manner, the surgeon should not withhold necessary surgery because of age alone. Anatomical incisions sutured with silk, linen, or cotton allow for early mobilization, and the delay in healing is usually due to other general factors already mentioned rather than age per se.

Allergy.—Allergy may produce a delayed healing or even premature absorption of catgut. Hopps found that hypersensitivity to catgut could be produced in rabbits and guinea pigs as shown by positive cutaneous reactions, positive reactions from implantations in the anterior chambers of the eye, and demonstration of humoral antibodies (precipitins, agglutinins, complement-fixing antibodies, and anaphylactins). There was an

In addition, it protects the body and, through glands, secretes important substances for body metabolism. It occurs in skin (stratified squamous epithelium), in the mucous membranes, and in the respiratory tract (pseudostratified epithelium). It is found in glands (breast) and glandular organs like liver and kidney (simple cuboidal epithelium). Epithelial tissue is perhaps the second best healing tissue; it will heal and replace itself, as we have seen in skin wounds. The epithelium which forms over an injured area, however, contains no sweat or sebaceous glands or hair follicles.*

Fig. 18.—X-ray photograph of a fractured femur, showing the formation of callus and the manner in which the continuity of the bone is reestablished, even though the reduction is not perfect.

3. Vascular tissue includes the blood corpuscles and the cells lining the blood vessels and lymphatics (endothelium). The blood corpuscles do not regenerate, although new corpuscles are constantly produced by a specialized organ, bone marrow, whose function it is to replace this tissue. The endothelial cells regenerate completely, permitting the preservation of vascular continuity after injury.

*The term *mesothelium* is applied to the lining of body cavities such as the pleura, peritoneum, and pericardium. These serous membranes are specialized loose connective tissue in a way. *Mesenchymal epithelium* is used to designate the lining of the subdural, subarachnoid, and perilymphatic spaces of the inner ear and the chambers of the eyeball. Joint cavities and bursae are lined by synovial membranes which contain epithelial cells and vary in morphology depending upon their underlying tissue—fibrous, areolar, and adipose. These simple squamous epithelial tissues which are mesodermal in origin heal readily.

4. Muscle tissue is highly specialized and does not readily regenerate itself. Striped muscle is mesodermal and unstriped mesenchymal in origin. The former has practically no power of regeneration; the latter cells retain some power of mitosis but regeneration is not seen after any major defect. If muscle is divided and sutured, it will join together, but not usually by muscle tissue. Surgeons will not cut across muscle, or suture it tightly, or include large amounts in the suture, because it heals with scar—not muscle tissue. In the abdominal wall the fascial coverings supply the tensile strength.

5. Nerve tissue is ectodermal. Animals have a certain number of nerve cells at birth (see Chapter 18)—some more, some less. These cells develop but do not increase in number. If the nerve cell is killed or injured, it never regenerates itself; it is gone forever. This is what happens to children with anterior poliomyelitis or infantile paralysis.

The more highly specialized the tissue, the less able it is to regenerate itself.

Repair as Seen in Specific Tissues

Bone.—

Bone develops late in embryonic life as a transformation of embryonic or adult connective tissue—after muscles, nerves, vessels, and many other organs are formed. Certain bones develop from connective tissue directly and are called membrane bones (intramembranous bone formation); others develop from cartilage and are called cartilage bones (endochondrial ossification). Spongy bone is first formed, and later it becomes compact through internal reconstruction. Membrane bones are seen in the face and the flat bones of the skull. These have a periosteum and two layers of compact bone, between which is the diploic cavity. Cartilage bones occur in the skeleton generally. The mandible is formed from Meckel's cartilage, which serves as a surface for the deposition of bone by connective tissue. The cartilage is later absorbed. Thus the lower jaw does not undergo endochondrial ossification. A long bone is composed of a diaphysis or shaft, an epiphysis or growing portion, and a metaphysis, which is adjacent to the epiphysis and is rich in blood supply. The metaphysis is important because here most infections occur and many new growths as well. It has a cortex made of compact bone and a medulla made of cancellous bone. The cortex is surrounded by periosteum, which, in the young, is composed of two layers—an outer fibrous one which carries vessels and nerves and an inner cellular layer which is filled with osteoblasts and has an osteogenetic function. The cancellous bone is lined by endosteum which is also osteogenetic. The compact bone is chiefly made of tricalcium phosphate, which lies betwen the meshes of interlacing collagenous fibers called *lamellae*. Some of these lamellae surround the haversian canals (Haversian lamellae). Within the canal are the artery and vein, connective tissue and fat cells, and some osteoblasts. Volkmann's canals also contain vessels but are not surrounded by concentric lamellae. Periosteal, interstitial, and endosteal lamellae are also seen as part of the meshwork, running in different directions. In the extremities the bone arteries run toward the elbow and away from the knee. Growth occurs at the epiphyseal ends, which are cartilaginous and ossify at various times in different bones, finally joining the shaft when growth is complete. The circumference of the bone grows from periosteum and endosteum. Some osteoblasts become enclosed in the matrix as bone cells and connect with each other through canaliculi.

When a bone is broken, a blood clot forms and fibrin is deposited There is an exudate and, in addition to the cells and collagenous material seen in superficial wounds, two special types of cells appear—*osteoblasts,*

which become osteocytes, and *osteoclasts.* The osteoblasts correspond to fibroblasts, but instead of forming collagen they form a soft substance known as *osteoid tissue.* This is laid down along the paths of blood vessels in trabeculae, at first transversely and later longitudinally, and serves to attract calcium salts.

The calcium phosphate which is deposited in bone apparently comes from adjacent bone rather than from the blood stream. Therefore, the administration of calcium by mouth influences bone formation only indirectly, for it must first be deposited in the storehouse of calcium (bones). These general principles are true of all injured tissues. *The cells which repair a particular kind of tissue come from neighboring tissues of like kind.* Such cells will usually appear in direct proportion to the adequacy of the blood supply and will *follow, not precede, the formation of the blood vessels. If inadequate,* granulation tissue will form and the defect will be healed by scar. If entirely absent, *repair cannot take place.*

Connective tissue may change to bone in adventitious sites in the connective tissue beneath the renal pelvis. If the epithelium of the urinary or gall bladder is implanted near dense connective tissue (in dogs), bone develops from the connective tissue (Bloom).

The osteoclasts correspond to macrophages and clean up the debris, permitting a re-establishment of the marrow cavity. The osteoid substance forms a bulblike mass around the broken ends of the bone known as a *callus.* In the early stages, the callus is soft, but later it becomes hard. The edges of the bone unite, forming new bone with a solid center. Scavenger cells called *osteoclasts* appear. They re-establish the marrow cavity of the bone. Bone may be laid down in connective tissue, as in the skull, or it may originate in cartilage, as in the long bones. Intermediary cartilage is mostly seen in the external portion of the bone. Drill hole observations reveal no intermediary cartilage. It is probably true that cartilage occurs in proportion to its need for temporary stabilization; that is, in incomplete fractures or a drill hole it is absent. In more complete injuries it is temporarily present. This hyaline cartilage undergoes degenerative changes when its usefulness is complete, disappears, and is replaced by bone. If the blood supply is poor, the continuity of the bone may be restored by fibrous tissue from surrounding structures or cartilage and may remain so. Thus we see that in healing, bone roughly retraces its formation and may stop at any stage, depending on its blood supply and other delays in repair previously enumerated. The skull heals by fibrous tissue only (thereby avoiding pressure on the brain by callus); the long bones, by connective tissue which is transformed into cartilage and then bone.

Intermediary cartilage degenerates due to the activity of mesenchymal cells and invading capillary loops. If such capillaries do not appear, the fracture may be healed by cartilage which is not replaced by bone. Dissolution of this cartilage is thought to be due to the action of blood vessel endothelium and "surrounding elements" which dissolve the interstitial substance in an unknown manner. Then the osteoid granulation tissue permeates the destroyed cartilage and changes it to bone through the action of the osteoblasts.

When a surgeon sets a bone, he must guard against the six factors previously described which delay healing.

Cartilage.—

Cartilage is a mesenchymal tissue developing from precartilage. It is made of homogenous, collagenous substance which is chemically a mixture of collagen, chondromucoid, chondroitin sulfuric acid, and albuminoid. In the many large spaces or lacunae are seen the cartilage cells (chondrocytes). These have been shown to contain glycogen. Cartilage grows by *interstitial* growth (production of more intercellular substance when the cells divide by mitosis) and by *appositional* growth (formation of new cartilage over the external surface). It is devoid of blood vessels. The nutritive fluid in the capillaries of the perichondrium must pass through the interstitial substance to reach the cells. A connective tissue envelope surrounds the cartilage—the perichondrium. Three types of cartilage exist: *hyalin cartilage*, which is found in the larynx, nose, trachea, bronchi, xiphoid cartilage, costal margins, and joints; *elastic cartilage*, which contains in its matrix yellow elastic fibers and is found in the external ear, auditory tube, epiglottis, and the small cartilages in the larynx; and *fibrocartilage*, which contains anastomosing bundles of fibers and is seen in the intervertebral discs, interpubic fibrocartilages, and in the sternoclavicular, acromioclavicular, and mandibular joints.

Cartilage heals slowly but completely. It is like bone in origin, being derived from mesenchymal tissue. It has no blood supply of its own and is nourished by surrounding tissues. It is a forerunner of bone. Due to its poor blood supply, inflammation and healing will be extremely slow. Cartilage has the ability to obtain nourishment from the surrounding tissue; hence it can be used in plastic surgery. It can be transplanted and will live. Repair takes place by a metaplasia of the loose connective tissue around the cartilage. Any connective tissue after injury may change to cartilage. Function may determine this in bone or cartilage. False joints in unreduced fractures may be lined by cartilage.

Intestines.—

The gastrointestinal canal develops from the foregut, midgut, and hindgut. It is composed of four layers, tunica mucosa, tela submucosa, tunica muscularis, and tunica adventitia (or serosa). The mucous membrane is laid down first from the mesenteron; later the connective tissue elements surround it. The esophagus and rectum do not have a serosa; they are surrounded by an adventitia of connective tissue. The blood supply comes from the mesentery and encircles the bowel, dipping into its layers closer to the mesentery in the small bowel and then large bowel, in which the vessels penetrate close to the antimesenteric border, almost surrounding the bowel wall on the outside. Gangene from distention is therefore rarely seen in the latter and commonly seen in the former.

The intestinal wall is composed of mucosa, submucosa, muscularis, and serosa. The submucous coat, which is found between the muscle and mucous layers, is the strongest coat in the intestine. This is the fibrous substance of which violin strings and surgical catgut are made. The serous coat is the quickest one to heal, but it will do so only when its cells approximate each other: that is, serosa to serosa. Therefore, in intestinal surgery the bowel wall is turned in. After one-half hour a deposit of fibrin occurs due to clotting of blood plasma; later a collagenous exudate forms and prevents leakage. If it were not for this, we could

not possibly do any intestinal surgery. Even the most delicate suturing would not prevent leakage and subsequent peritonitis were it not for the astounding ability of the serous coat to seal itself so rapidly and completely. This must be remembered in surgery on the esophagus or rectum which are devoid of serosa and therefore heal less readily. The inner coats are sutured first (the muscularis is of minor importance in repair) and then turned in. They heal by second intention because they slough or become infected. However, infection may be reduced by the use of succinylsulfathiazole or phthalylsulfathiazole (Sulfathaladine) preoperatively. (See Chapter 5.) The serous coat heals by granulation from the subserous connective tissue. This begins in twenty-four hours and is complete in about a week. The inverted serosa is absorbed. Food and water are withheld for about four days, so that the inner coats may

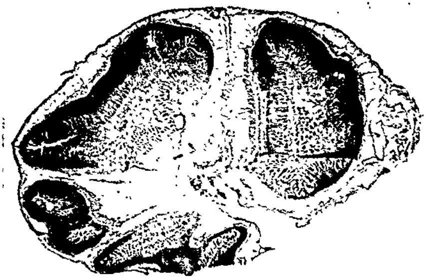


Fig. 19.—Healing of intestines (dog). Section was made on seventh day after suture of intact loops of bowel. Note large amount of fibrinous exudate. Organization has begun. The serous coat is undergoing absorption.

form healthy granulation tissue before being subjected to the stress of digestion. (Although with the use of the Levine and Hiller-Abbot tubes and suction, fluids may be allowed by mouth after twenty-four hours.) The mucous membrane is regenerated, including some of its glands.

Muscle.—

Skeletal muscles develop from mesodermic somites. Muscle tissue is highly specialized and has contractile power. Each muscle fiber has a sheath (sarcolemma), which surrounds the cytoplasm (sarcoplasm) and the peripherally placed nucleus. The sarcolemma is one micron thick. It is a structureless membrane derived either from the muscle cell or the connective tissue surrounding the muscle fibers. The myofibrils are arranged in fields (Cohnheim's areas), muscle columns, or sarcostyles. When viewed in cross section, muscles appear to be divided into bundles or fasciculi by connective tissue, which ultimately blends with the sarcolemma around the individual muscle fibers (internal perimysium or endomysium). This, in turn, is derived from the capsule of the muscle (external perimysium).

Muscle tissue may undergo hypertrophy but not hyperplasia. Therefore, muscle tissue, striped or unstriped, does not regenerate itself when destroyed. It therefore fills in with scar tissue derived from the external and internal perimysium. Striped muscle has almost no power of regeneration. Unstriped muscle cells do have the power of mitosis. However, regeneration is not noted except in very small wounds.

Tendons.—

Tendons consist of very dense connective tissue with collagenous fibrils, bound into bundles in a matrix containing tendomucoid. Very little elastic tissue is present. The bundles or fasciculi are separated by septa. Their peritendineum surrounds the tendon and gives rise to these septa. Many tendons have sheaths surrounding the mesotendineum which carries the blood supply. Tendons are attached to muscles and bone. The collagenous bundles of the external perimysium pass directly over into those

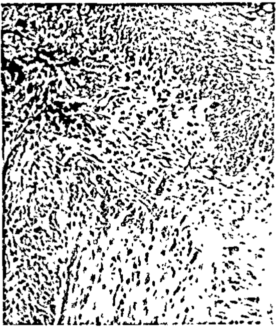


Fig. 20.—Repair of muscle (rabbit's tongue). Muscle fibers have been replaced by fibrous tissue.

of the tendon; the sarcolemma covering the rounded, cone shaped ends of the muscle fiber is fused with the ends of the collagenous bundles. Tendons are attached to bone through the periosteum. At such sites may be found Sharpey's fibers which are also collagenous bundles of varying thickness passing through the systems of lamellae in different directions.

Tendons heal very quickly and completely and may be divided, lengthened, shortened, or transplanted. They are mesenchymal tissue and heal as well as connective tissue. Silk is used as the suture material and the sheath is closed. Early motion was formerly advocated to prevent adhesions. This was a fallacy because repair takes place as in other related tissues. Softening occurs immediately after suturing, and stitches will pull out unless fibroplasia is well established (fourteen days). Usually *three to four weeks in splints is necessary for complete repair.*

Blood Vessels.—

Blood vessels are composed of three principal layers: *tunica intima*, which includes the endothelium and, generally, an underlying elastic membrane; the *tunica media*, which is primarily a layer of circular smooth muscle fibers (relatively thicker in the arterioles and thinner in the larger arteries, where elastic tissue is more common); *tunica externa*, or *adventitia*, which is chiefly connective tissue and carries the blood supply (vasa vasorum) and the nerve supply. Veins are like arteries except that their walls are thinner and they have valves. *The external coat of veins is better developed* and the muscle coats contain more longitudinal muscle fibers.

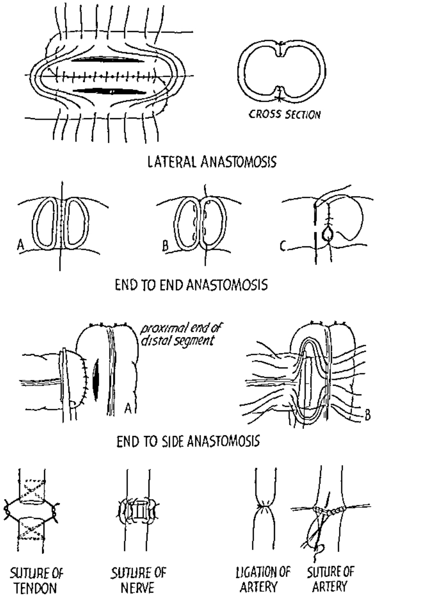


Fig. 21.—Diagram illustrating methods of repairing intestine, tendon, nerve, and artery. The intestinal suture is placed so that the serous coat will be inverted, approximating serosa to serosa. The method shown for tendon is designed to catch the longitudinal fibers, so that the ends will remain in approximation. The nerve is sutured with *stitches through the epineurium.* In the repair of blood vessels it is important that intima be approximated to intima. This is accomplished when simple ligation is done or when vessels are sutured by an eversion running mattress suture. At times this is not possible, as in the production of an artificial ductus by anastomosis of the pulmonary artery and aorta. *In this instance the posterior suture line is a continuous over* and over. Some surgeons use an eversion mattress suture interrupted followed by a continuous over-and-over stitch. This type is employed in anastomosis of the aorta following the excision of a coarctation. However, good results are obtained by a continuous over-and-over stitch.

Blood vessels are composed of intima (endothelium), media (muscle), and adventitia (connective tissue). If the lining of a vessel is roughened, a clot (thrombus) will form. In wounds of blood vessels this takes place and is nature's way of arresting hemorrhage. If the surgeon ligates a vessel he approximates intima to intima, and healing with regeneration occurs. Suturing of vessels is now a common practice. Should it be necessary, the finest silk (00000 on atraumatic or swadged on needle) *should be employed and the intima should be sutured to intima. Indications* and conditions for successful arterial suture are as follows: The vessel should be large with few collaterals; it should not be diseased (arteriosclerotic); the wound should not be infected; the divided ends cannot be too far apart, producing tension on the suture line. Best results are seen when the vessel is only partially divided (up to 50 per cent). (See Chapter 17.)

Nerve Tissue.—

Nerve tissue is derived from ectoderm and its unit is the neuron. The neuron is composed of the nerve cell, its dendrites, the axis-cylinder (which may be surrounded by myelin), and the neurolemma or sheath. The axis-cylinder in myelinated nerves is centrally placed. The nerve sheath or neurolemma (sheath of Schwann) shows at frequent intervals annular constrictions—the so called nodes of Ranvier. This structure is probably not connective tissue but a membrane similar to the sarcolemma (q.v.). Nuclei occur in the neurolemma midway between these nodes. Around the peripheral nerves is a connective tissue sheath (epineurim). Within this layer nerve cords are grouped and held together by the perineurium, which in turn divides the neurons into groups by an inward prolongation (endoneurium) or "sheath of Henle." Thus a nerve on cut section is seen to have a pattern which should be matched when cut nerves are sutured.

A nerve cell (neuron) is composed of a cell body and an axis-cylinder. In so-called myelinated nerves the axis-cylinder is surrounded by myelin and a neurolemma, or sheath of Schwann. (Myelinated nerves include motor nerves and sensory nerves peripheral to the posterior ganglia.) If the axis-cylinder is not myelinated and surrounded by neurolemma, it will not regenerate.

Division of nerve fibers in the spinal cord is not followed by regeneration except in very young experimental animals. Motor nerves do not assume their myelin sheaths until they leave the cord. Sensory nerves have no myelin central to the spinal ganglia. Although myelin is formed in the medulla spinalis, the nerve fibers in the cord have no neurolemma and this is probably responsible for their failure to regenerate.

We have said that a nerve cell will not regenerate itself. If a nerve fiber is injured, its sheath will repair itself as do other tissues, but the axis-cylinder will form only by new growth from the cell body. After the axis-cylinder is cut, it degenerates and breaks down into granules (Wallerian degeneration). This process extends peripherally to the end of the nerve and centrally to the next node of Ranvier. The myelin sheath disintegrates into fatlike droplets which are finally absorbed. The nuclei of the Schwann cells multiply and line up in rows parallel to the axis-cylinder. The cell body may show Nissl's granules. Although

the surgeon does not suture each neurolemma, he does approximate them when he sutures the epineurium of a nerve. Then the new nerve fiber grows down the empty sheath.

Advantage is taken of this fact in extensive injury of nerve. For example, in the repair of the facial nerve an empty sheath is inserted between the cut ends of the nerve. This sheath is obtained by dividing the anterior cutaneous nerve of the thigh, allowing the axis cylinder to degenerate and then removing a portion of the distal end of the nerve.

The only thing that heals by intention is the sheath (that is, any type of intention, be it first or second); the axis-cylinder grows down this sheath if the cell body is uninjured. To re-establish function in the nerve, the axis-cylinder must grow all the way down. If it is a long nerve (as the sciatic), it may take a year for it to heal and for function to be restored. A complex nerve (such as the ulnar) is less apt to regenerate completely than a simple nerve (such as the radial), and an almost purely motor or sensory nerve regenerates better than a mixed nerve. Should the regeneration of the axis-cylinder be interfered with by scar *tissue, the nerve will curl at the end, forming a painful bulblike swelling* called a *neuroma.*

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thelial cells have more bacteria and the converse is true. These cells engulf but do not always destroy microorganisms. Bacteria have been found in the lining of the stomach, but in most cases they are destroyed by the hydrochloric acid in the gastric juice. Practically every tissue in the body, then, may contain bacteria, but their mere presence does not constitute an infection or a disease. Also, as in the soil, very few tissues contain only one type of germ and if infection occurs many strains may be responsible. It is the natural or acquired immunity to these organisms that keeps us in a healthy state (q.v.).

IMMUNITY

Immunity may be defined as a state in which the body is resistant to a specific bacterial or virus invasion. The word resistance is a relative term and implies a general strength against bacteria. It is that inherent quality of healthy tissue which makes it an unfavorable site for bacterial growth. Various kinds of immunity are known: (1) *local* (in individual tissues and their cells); *general* (through the antibodies of the blood; (2) *natural* (inborn); *acquired* (as a result of experience with the disease, of maturation, or of vaccination; (3) *active* (produced by the individual's own forces); *passive* (conveyed by injection of immune sera).

Local immunity is applied to the resistance of the tissue cells at the site of the infection. There is no doubt that local tissue immunity is very important, if not the most important, part of our resistance to disease.

Walsh and Cannon found that they could immunize rabbits against pneumococci by local vaccination with formaldehyde-killer or autolyzed pneumococci. Since there were no demonstrable antibodies in the blood stream, they considered the immunity to be entirely local.

Wood has described three histologic zones in pneumonia: an outer zone filled with edema fluid in the alveoli; few leucocytes, and many pneumococci which multiply here and spread the lesion. Inside this zone the alveoli contain many leucocytes and bacteria. A feature here was that there were less bacteria and more leucocytes the more central the area. Polymorphonuclears were ingesting the organisms. The central zone is characterized by consolidation due to fibrin and leucocytes, no microorganisms, and, in the older portion, macrophagic resolution.

The mechanism of the therapeutic arrest of pneumonia by the use of immune serum is due to agglutination and immobilization of the pneumococci by alveolar adhesion. This may be due to specific epithelial opsonins very much like so called "endothelial opsonins."

Mesothelial-lined cavities owe some of their resistance to serous fluids. These not only dilute toxins but contain freely floating cells which are macrophages and correspond to polyblasts in inflammatory exudates. Desquamated epithelial cells may turn into fibroblasts. Small lymphocytes may become macrophages. These cells with their primitive ability to differentiate aid in establishing a high degree of local resistance.

The intact skin has always been thought to be an impermeable barrier to bacteria. This is probably true, but recent studies have shown that virus (lymphocytic choriomeningitis) may penetrate the intact skin of guinea pigs. Thus we have experimental confirmation for our practice of giving antirabic vaccines to persons who have been licked or otherwise contaminated by the saliva of rabid animals or patients (see Chapter 7).

Chapter 4

BACTERIAL INVASION—THE REACTIONS OF TISSUES AND THE BODY AS A WHOLE TO BACTERIAL INJURY

Bacteria may be found almost everywhere.

Spores are found even in the stratosphere, where the ordinary flora of the air are not encountered. However, spore-bearing bacteria, when taken up into the stratosphere from earth, survive. Organisms are said to live in symbiosis (cannot exist independently), mutualism (both are benefited), and mensolism (one is benefited, the other unaffected).

The physician must be constantly alert to the danger they present. Microorganisms are not all harmful. *Saprophytes* are those bacteria which live on dead or decaying matter; *parasites* are those which thrive on living matter. The saprophytes cause certain ferments to form in the intestinal tract and probably aid in the digestion of food; coliform bacteria aid in the formation of vitamin K_2 in the colon. Dirt and soil contain virulent anaerobes; various species of bacteria, fungi, actinomycetes, and genera of algae; all types of protozoa, nematodes, worms, insects, and viruses. These microbes carry out their activities in the variegated fauna and flora which is usually present in soil. They may act in symbiosis, aiding one another in useful functions (fixation of atmospheric nitrogen, production of nitrite from ammonia, decomposition of proteins or cellulose), or they may inhibit each other by the production of antibiotic substances (penicillin, streptomycin, aureomycin, tyrothrycin, gramicidin). Virulent anaerobes make dirty wounds dangerous. Experimental animals living in an aseptic environment do not thrive very well. There are germs all through the body, particularly in cavities or ducts which communicate with the outside, such as the mouth (around teeth and tonsils), the nose, the vagina, the rectum, and the urethra. The deep layers of the skin (glands), muscles, liver, kidney, and other parenchymatous organs are also inhabited by bacteria.

These bacteria are mostly gas-producing anaerobes which are harmless when injested into experimental animals. However, they may become virulent when contaminated with ''transient'' organisms. The gastrointestinal tract of the newborn is free from bacteria for the first five to ten hours. This was determined by us in operations for imperforate anus. However, we have operated upon infants within the first five hours of life, opened the blind hind-gut, and found coliform organisms.

The only tissues which are supposedly free from bacteria are the brain and spinal cord, heart muscle, cartilage, cortical bone, tendon, and the eye chambers. Those organs having an abundance of reticulo-endo-

It is due to the presence of phagocytic cells, such as tissue wandering cells, macrophages, and all reticulo-endothelial cells, as well as to migration of leucocytes and to chemical substances (leucoprotease, lymphoprotease, erepsin-like substances) elaborated by the leucocytes which have the power of inhibiting the growth of bacteria or rendering them more susceptible to phagocytic destruction. Local immunity is also aided by lymphatic fibrin plugs and immune bodies (opsonins). This explains why certain contaminated tissues may heal by first intention (vagina, rectum, mouth), although when traumatized severely they do not always do so. If strong antiseptics are employed, local resistance is so reduced that a wound is considered as infected even if seen early. Some tissues such as the pleura and peritoneum have by nature a high degree of immunity. Others possess this because of good blood supply (face). One may contaminate a clean wound after eight or ten days with staphylococci without producing a general infection (local immunity). Healing by second intention takes place only after local immunity has been established.

General immunity is also extremely important in our defensive mechanism.

Pfeiffer was one of the first to show the ability of an immune animal to destroy bacteria, as distinguished from the power to neutralize their soluble toxins which had been shown by Ehrlich. When cholera spirella were injected into the peritoneal cavity of cholera-immune guinea pigs, the microorganisms swelled, became granular, and under went solution. When the bacteria were injected into a normal animal along with a sufficient dose of cholera-immune serum, the same effect was produced. However, in the unprotected animal death invariably resulted.

It has long been known that virus diseases especially infantile paralysis, seem to affect well-nourished children. Recent experiments show that the rate of intradermal spread of virus varies inversely with the amountof interstitial water: increased amounts of interstitial fluid reduce the rate of spread and dehydration increases the rate and area. Depriving rabbits of food was found to increase interstitial fluid. If they were given plenty of water, their resistance to vaccine virus was increased.

It is chiefly humoral and is thought to be due to chemical substances in the blood known as antibodies. Depending upon their mode of attacking toxins or bacteria, they are called agglutinins, precipitins, bacteriolysins, opsonins, alexins, or antitoxins.

These protective antibodies are newly formed chemical substances which are synthesized within the cell Precipitins are normal serum globulins synthesized intracellularly and altered by the "templating" action of the absorbed antigen. This antigenic template is synthesized from intracellular protein reserves. Thus ample *protein reserve* means an ample supply of antibodies in most instances. Normal antitoxic resistance to diphtheria toxin is quadrupled on a high protein diet.

Formerly there were two schools of thought concerning immunity. The "cellular group," headed by Metchnikoff, thought that local cells played the most important role; the "humoral group," led by Ehrlich, believed that antibodies were more important. Today we know that both play important roles in defense reactions.

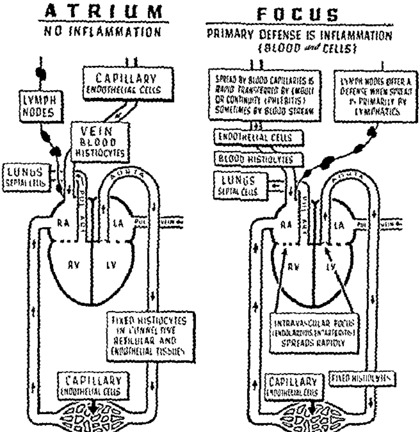

Fig. 22.—Diagram illustrating the dissemination of infection from an *atrium* and from a *focus* of infection. Note that there is *no inflammation* about an atrium so that there is direct access to the lymph or blood capillary. The lymph method of dissemination offers an early line of defense in the *lymph nodes* and the endothelial cells of the tubular lymphatics. Ultimately, bacteria gain entrance to the venous system through the right lymphatic duct or the thoracic duct on the left. From here bacteria may be carried through the right atrium, right ventricle pulmonary artery to the lungs. Here the septal cells remove some of the bacteria. The rest find their way through the pulmonary vein to the left atrium, left ventricle, and the arterial system. Here the bacteria are removed by the fixed histiocytes in connective, reticular, and endothelial tissues. In addition, endothelial cells in the capillaries as well as wandering histiocytes in the blood stream aid in the elimination of bacteria from the circulating blood.

Should bacteria gain entrance through the blood capillaries, dissemination would be more rapid. Although the endothelial cells of the capillaries and the blood histiocytes attempt to remove entering bacteria, the veins carry the blood directly to the heart; then the circulation and removal of bacteria from the blood stream is the same as discussed above In either event bacteria are removed by the reticulo-endothelial system so that actual growth of the microorganisms probably does not take place within the blood stream unless the reticulo-endothelial system is completely filled or blocked.

This is usually a terminal event in the human being A blockade of the reticulo-endothelial system can be produced experimentally with dyes. Such animals develop a fatal bacteremia quickly after the injection of virulent organisms.

A *focus* of infection implies an inflammation. Here a primary defense is set up composed of blood and cells (inflammation) as described in the text. From this focus, bacteria may spread in two ways: (1) by blood capillaries and (2) by the lymphatics. The spread by blood capillaries may be rapid and may be transferred to distant areas by emboli or to neighboring regions by continuity (phlebitis). Sometimes the spread occurs by the blood stream itself in late cases. Should the focus be within the blood vessel, as in *endocarditis* or *endarteritis*, the *dissemination of bacteria is continuous* and severe. Lymph nodes offer a defense to the spread from a primary focus by way of *the lymphatics and, therefore, are more apt to halt the onset of bacteriemia.* In either instance, once bacteria reach the blood stream, the method of removal of microorganisms *is the same as described under atrium.*

These concepts explain variations in temperature and leucocyte counts as well as the *finding of positive and negative blood cultures in the presence of a bacteriemia.*

Active immunity is the same as *acquired immunity* and is the result of experience with the disease or vaccines; in other words, the patient fights his own battle with his own blood and cells. Passive immunity is conferred upon the patient by the use of immunizing serum, such as diphtheria antitoxin or tetanus antitoxin. Absolute immunity is rare and practically unknown in man, although there are very few diseases to which he has no immunity (for example, glanders). Dogs are supposed to have an absolute immunity to leprosy.

VACCINES AND IMMUNIZING SERA

Vaccines are substances made from attenuated or killed bacteria or their toxins. They are injected to produce active immunity, and they are used chiefly to prevent disease, but, in some instances, they are used to raise resistance in chronic diseases. Examples of the former are *typhoid fever and smallpox vaccines. Examples of the latter are staphylococcus* and pertussis vaccines.

The Kruger method of producing pertussis vaccine is a mechanical grinding process. Vaccines may also be made by ultraviolet irradiation. Toxoids are made by the addition of formalin to bacterial toxins and then incubating the mixture for thirty days. In addition, adjuvant substances such as alum may be added or the vaccine (in diphtheria and tetanus) may be included.

Vaccines may be either *autogenous* or *stock*. The autogenous are made from the patient's own pus; the stock, from laboratory cultures.

Immunizing serum is derived from animals that have been made actively immune to the disease by repeated injections of the organism. Such animals produce antibodies against the disease until they are immune. Their blood is then drawn and the serum is injected into the patient, thereby transplanting these immunizing bodies. This confers on the patient a passive immunity. Human immune serum is used in scarlet fever. Placental extract is rich in immune globulin and is used to prevent measles as well as other diseases.

Anaphylaxis.—Patients who have received injections of serum of any kind are rendered susceptible to the protein and, when given a second dose, may develop severe symptoms resembling shock. These may be so severe as *to cause death. If a local necrosis occurs at the site of the in*jection, it is known as the Arthus phenomenon; if general symptoms occur, the condition is called *anaphylaxis* or *anaphylactic* shock. If the symptoms develop only after eight or ten days, they are mild and consist of fever, lymphadenopathy, joint pains, and hives. This is known as "serum sickness"

(*Ana*, against; *phylaxis*, protection.) Besredka believed that anaphylactic shock does not occur under anesthesia because of the depressed sensitivity of nerve cells. Auer and Lewis believed that anaphylaxis is due to spasm of the bronchioles and is not of central origin. We have observed this bronchiolar spasm in our experiments. Dale thought it due to histamine. My colleagues and I have been able to produce anaphylac-

Immunity may be natural or acquired. An example of the former is the resistance which some individuals have to particular diseases as result of racial or hereditary factors, such as the resistance of natives of the tropics to yellow fever and the lack of resistance of the American Indian and Negro to tuberculosis. This is perhaps only partially hereditary. Experience with the disease early in life, survival of the fittest, and the inherited environment all play a role. Acquired immunity is the immunity that occurs as a result of experience with the disease, either in its active form or in a mild form produced by vaccines. Examples such as scarlet fever and diphtheria immunity may be cited. Some believe the rarity of childhood diseases in adults that have not previously had them is due to a mature immunological panel (see Chapter 10).

Experiments tend to show a sudden and great increase in prenatal immunity at the time of birth. We have found that the newborn stands surgery well and his microbic resistance is equal to that of older groups provided water and food balance are maintained.

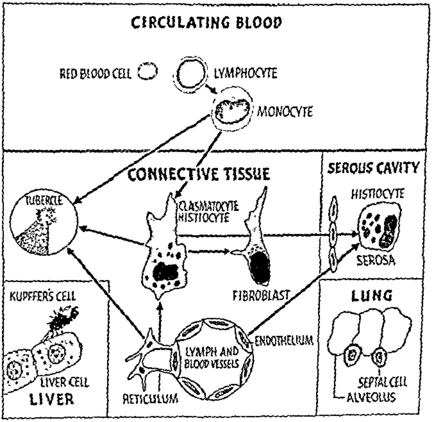

Fig. 23.—The reticulo-endothelial system. (After Gay: J. A. M. A. 97: 1193, 1931.) The principal sites of the cells and their possible derivations are indicated. The fibroblast only forms collagen and does not give rise to other cells. The epithelioid cells around the tubercle may be one source of fibroblasts. Most cells of the body may become phagocytic and in this sense are part of the reticulo-endothelial system. The reticulo-endothelial cells or histiocytes are usually divided into those which are fixed and those which are wandering. The fixed varieties are found in connective tissues, reticular tissues in the spleen, lymph nodes, and bone marrow, endothelium everywhere, lining of blood sinuses, "Kupfer cells" of the liver and especially endothelium of the spleen, bone marrow, adrenal and pituitary, and microglia. The wandering histiocytes are found in the tissues and in the blood stream. The latter may be of extraneous origin or the monocytes.

Local Effects of Infection.—*Inflammation* is the reaction of tissues to injury. The injury may be due either to simple mechanical trauma or to bacterial invasion. In either case, the tissue reaction to this insult, which is mechanical and cellular, denotes its presence. There are infections that are so overwhelming that the patient has very little reaction; fortunately this condition is rare. If the infection is due to a certain specific organism calling forth a characteristic reaction, it is known as a *specific infection* (for example, tuberculosis of the adult type). This means that the body will react to that particular organism in a certain manner. If the infection is produced by various organisms calling forth no specific type of reaction, it is said to be a *nonspecific infection* and is just like an irritation produced by trauma. The type of bacterial invasion is recognized by the defense reaction it excites, as well as by finding and culturing the *organism which is rarely of one type or strain. The concept of* specificity is probably inaccurate (see page 73).

When an inflammation occurs, *active hyperemia* is first noted due to the dilated capillaries carrying more blood and cells to the part. This occurs in response to any form of trauma and initiates the body's defense against it. Then *exudation* takes place. At first plasma, then after a few hours blood cells, go out into the field of the infection. This is due to increased capillary permeability in the dilated vessels at the site of infection. The loss of plasma prevents reabsorption of toxins because the osmotic pressure in the tissue spaces becomes greater than that in the vessels. Absorption can then only take place through the lymphatics. The lymphatic vessels, in turn, are occluded as intercellular pressure becomes increased, and within twenty-four hours, due to endothelial injury by the bacterial exotoxin, thrombosis and fibrin deposits are present in the lymphatics. Within forty-eight hours stasis occurs within the lumen of the blood capillaries. This is due to the loss of plasma and the packing of the capillaries with cells. After the fourth day thrombi appear in the blood capillaries also.

Thorsness and Higgins injected 10 c.c. of an 8 per cent solution of aleuronat subcutaneously into rabbits. Graphite was then injected on the fifth day. At autopsy none was found in the enlarged regional nodes. Sections of the walls of the abscess showed a network of fibrin from the first day, which began to break up by the eighth day. After this time (about the sixteenth day) graphite began to go through. Vitally stained macrophages (trypan blue) became evident by the second day and completely surrounded the abscess by the fifth day. Soluble substances such as phenolphthalein and epinephrine were well absorbed around the abscess, but in the abscess, after the fourth to sixth day, very little was absorbed (due to blockage of blood capillaries). This capillary blockage occurs later due to the fact that the neutrophiles reached their height by the second day; after this they decreased and the mononuclears (large lymphocytes, monocytes, histiocytes) increased, reaching a maximum after the fifth day. The influx of the polyblasts from the blood and surrounding tissues helped to block the capillaries.

tic shock in guinea pigs under ether anesthesia, although we have never seen it occur in human beings under anesthesia. Quill reports a single human case and many laboratory experiments to show that either does not protect against anaphylaxis. Many theories have been advanced to explain anaphylaxis:

1. A lysate is elaborated by the tissues after the first dose. A second injection causes a reaction due to excess lysate, which releases toxic fractions of protein.

2. The union of too much antigen with too little antibody. The latter is incapable of destroying the former but is capable of converting the inert protein into one which stimulates smooth muscle and acts like a poisonous substance, as does partially digested protein when given parenterally. This zone of incomplete immunity, whether on its way up or down, is the danger zone.

3. The resistance curve reaches its height in about eight days and then declines. If given during the ascent of the curve, the second dose of serum causes no reaction; if given during the descent, it causes anaphylaxis.

4. Moon believes the physiological disturbances are comparable to those which occur in peptone shock. *The reaction is cellular rather than humoral; the meeting of antigen and antibody within the cells irritates and injures them.* The capillary endothelium is the chief point of injury. The loss of tonus makes the capillaries become more permeable, and plasma is lost.

5. Perhaps the Arthus phenomenon is due to the local increase in capillary permeability resulting from the previous injection of protein.

6. Eclampsia has been ascribed to heterologization of placental protein and also to maternal isolysins formed against paternal Rh agglutinogens in fetal blood.

7. Bronchiolar spasm gives rise to anoxic anoxemia which may cause increased permeability of capillaries, loss of plasma, compensatory vasoconstriction, more loss of plasma and fluid, hemoconcentration, stagnant anoxemia, and shock. If this is true, oxygen and plasma would be of great help.

Individuals may be sensitive to proteins other than those in sera, such as pollen of plants, horse dander, certain proteins in foods, or bacteria and fungi. The latter may manifest themselves as local or distant reactions; "-id" allergy (tuberculid, epidermophytid) may remain until the primary site is cured. Even crystalloids and drugs may produce reactions (aspirin, arsenicals, etc.). Such sensitiveness is called *allergy* (literally, "other work"). It is therefore necessary to inquire of a patient, before giving serum of any sort, whether he has an allergy (as evidenced by asthma, eczema, migraine, hay fever, hives, or sensitivity to horses, and whether he has had serum before. When it becomes necessary to give serum under any of these conditions, it should be administered in small divided doses to prevent any serious reaction. Should a reaction occur, adrenalin and the nitrites are perhaps the best drugs to use. In addition, oxygen and plasma, if available, may help.

EFFECTS OF BACTERIAL INVASION

Contamination implies the presence of bacteria. **Infection** means not only the presence of bacteria but their rapid growth and destruction of tissue as well. Saprophytic infection may be midway between, implying the growth of the organism without invasion and destruction of tissue. Most microorganisms depend upon the destruction of tissue to exist and multiply.

capillaries begins to form but is destroyed by the bacterial toxins until a new granulation tissue creates an environment which is unfavorable for bacterial growth and invasion (local immunity). The thrombi in small vessels occur before granulation tissue is formed and remain until it is formed without being destroyed; then new capillary loops appear and the thrombi retract and become absorbed. However, by this time local immunity is established and surgical intervention or spontaneous evacuation of pus occurs. If pus is not evacuated, the granulation tissue behaves as it always does; that is, it cicatrizes and forms a scar. This scar forms a connective tissue wall which surrounds the cavity of pus, giving rise to an inflammatory cyst. It becomes a cyst because the pus becomes sterile and undergoes liquefaction.

The destruction of tissue at the site of an infection is not all due to bacteria. Autolysis occurs as a result of trypsin and pepsinlike enzymes which are liberated by dying cells. Heterolysis results from three enzymes. Leucoprotease is said to be produced by polymorphonuclear leucocytes and digests protein in an alkaline medium. Lymphoprotease is a product of the lymphocytes. It digests protein in an acid medium. Erepsin-like substance is also a product of the granular leucocytes and is said to act on proteoses. These enzymes are created by the cells to remove dead tissue and digest unhealthy tissue and thereby facilitate the spontaneous evacuation of an abscess. They may act within the polymorphonuclear leucocyte, thereby permitting the digestion of cellular debris and bacteria which they have engulfed. An antienzyme exists in the blood serum inhibiting the action of enzymes. Heterolysis does not occur, therefore, in untraumatized tissues.

Since bacteria thrive on the products of proteolysis, it would seem that this enzymic action is helpful to the invading microorganisms. It is also known that such products of proteolysis contain antisulfonamide factors (para-aminobenzoic acid). The more leucocytes, the more enzymic action. Since the enzymes do not affect healthy tissue, they simply clear the area of unhealthy cells, permitting the leucocytes to act and probably making bacteria more vulnerable for such action. In fact, certain enzymes are now being used (experimentally) to aid in the annihilation of bacteria (see Chapter 5). Since the leucoproteases do not affect untraumatized tissue, they do not in any way interfere with the process of localization. Sulfonamides could not enter and are not needed in such an area (see Chapter 5).

On the other hand, if the individual is weak, the infection is disseminated and may result in an overwhelming bacteriemia.

Different clinical types of infection are classified according to their length of duration as (1) *acute*, (2) *subacute*, and (3) *chronic*.

Harvey and Hamilton proved an invariable sequence of events in response to the entrance of foreign material into the body: first there appeared polymorphonuclears, followed by monocytes, and in time by lymphocytes. There is a chemotaxis which calls cells to a focus but not special kinds of cells. This depends on acuteness or chronicity, local tissue destruction, and duration of stimulus rather than on a specific reaction of the tissues to different types of stimuli. This is well exemplified in bone infections where an acute tuberculous infection may resemble that of the pyogenic organisms and a chronic staphylococcic type of infection (Brodie's abscess) may mimic tuberculosis.

Acute infections arise and develop rapidly. They are usually caused by a single successful invasion of the organisms and may be severe. The blood stream may be continually or continuously flooded with bacteria. They are either overcome by the patient in a relatively short time or cause death. *Subacute* infections are never severe and yet may produce

As a result of these processes infection is walled off. Experiments have shown that crystalloids injected into the infected area of an experimental animal are not absorbed. When a colloid such as India ink is injected into the center of an abscess it is not found in the neighboring lymph nodes even after the second day because the lymphatics are occluded, preventing the absorption of colloids. The ink remains within the abscess. This is the process seen in the localized infection and is usually associated with staphylococcus invasion (q.v.). In the more severe streptococcic infections these localizing factors are not seen and there results widespread destruction of tissue, with systemic absorption (see Chapter 5). In the center of this area of activity there is destruction of tissue.

Tissue cells are killed by the action of bacterial toxins. This destruction of tissue, or *necrosis*, will continue as long as the bacteria proliferate and invade the tissues. In pimples the area is small; in boils and carbuncles, much larger. In diffuse infections it is extremely large. Within the area of destruction many cells are found; these are the polymorphonuclear leucocytes; later macrophages and monocytes appear. Accumulations of large numbers of cells finally fill the cavity. This process is known as *suppuration* (formation of pus).

As we have learned in Chapter 1, surgeons during the Middle Ages spoke of "laudable pus." Properly interpreted, pus is laudable and indispensable in the control of severe infection. If a patient is not overwhelmed by an infection in two or three days, the reaction which we have described occurs. Surgeons have always known this and have therefore preferred wounds which suppurated (staphylococcus?) to those which did not (streptococcus). The practice even existed of inducing suppuration by setons. This, of course, is no longer condoned. Pus is a fluid made of tissue debris, leucocytes, and their enzymes. These are nature's agents for the destruction of bacteria, the digestion and removal of necrotic material, and the irrigation of the area. This is the rationale for the modern treatment of infected wounds. Pus under pressure favors absorption and the separation of septic emboli. Therefore, incision after localization is all that is necessary. Pus will loosen and digest necrotic tissue. Anything interfering with this process thwarts the mechanism; therefore, irrigations, packing, and strong antiseptics should not be used. In fact, *rest* to the part and *avoidance of trauma* through massage and active motion will delimit lymphatic absorption. Therefore the treatment necessary in any infection is rest plus drainage after localization, with general supportive treatment (water balance, blood transfusion, etc.) and perhaps sulfonamides or penicillin in streptococcic and sulfadiazine in pneumococcic infection.

If the individual is strong and his fighting forces are active, *local immunity* occurs; then healing takes place by second intention.

We have previously shown (Chapter 3) that the granulation tissue in an infected area is like that between the edges of any wound healing by second intention. Let us examine a contused wound made by a blunt force. There would be very little bleeding, for the crushing force stimulates early thrombosis in the vessels. Then the sequence is hyperemia, exudation, granulation tissue, vascularization, and repair. The bacterial infection causes destruction of tissue cells and the process is the same. Thrombi may appear in the capillaries within forty-five minutes. Granulation tissue along with new

The vascular response to an irritant may be completely absent in rabbits with staphylococcic septicemia. This is probably due to a diminished circulation in the small blood vessels of the skin due to vasoconstriction which does not permit leucocytes or dyes to reach the area. The same phenomenon appears in shock from hemorrhage or other causes.

If no leucopenia exists, the foregoing explanation may mean that leucocytes are fighting the bacteriemia in more vital areas than the skin. Indeed they may exist in the peritoneal cavity, for example, in such large numbers as to produce a relative leucopenia.

Patients stand surgery poorly in the presence of severe septicemia. Therefore, operative intervention is limited to the relief of the focus of infection, and the operative procedure should always be as innocuous as possible. Children with measles or scarlet fever may develop a gangrenous stomatitis from the extraction of a tooth. However, the important fact is the general condition of the patient rather than the septicemia. If careful attention is given to water and electrolyte balance, proteins and carbohydrates, blood and plasma, as well as to vitamins, surgery can be made safe in the presence of a bacteriemia. Formerly typhoid fever was treated by starvation diets. Such patients did not react favorably to surgery. Now they are well fed and surgery is safe. It is therefore not so much the presence of bacteria as it is their interference *with vital functions that delays or prevents a proper inflammatory response to injury.*

Treatment of local foci by surgery in the presence of septicemia should be preceded by attention to the two factors which interfere with local inflammatory reactions; namely, the general condition of the patient as to nutrition and water balance and the showers of bacteria in the blood stream. Fortunately both are amenable to treatment, the former as indicated above, the latter by antibiotics (penicillin, streptomycin, aureomycin), and chemotherapeutic agents (sulfonamides).

In addition to redness there is heat (calor). Physicians speak of "hot" infections as opposed to the "cold" ones seen in tuberculosis. An infected area actually feels hot. However, if we take the patient's temperature (per rectum) and then take the temperature at the center of the infected area, it is about the same. The field of infection is hot, but *the temperature is the temperature of the blood. The blood surges* through this field so rapidly and in such quantity that the surface temperature is much higher than that of other skin areas; therefore, by contrast, it feels and is hot.

The third symptom is pain (dolor). The patient is in pain, because the tissues are stretched by the exudate, and the tension produced by this pressure, plus the effect of bacterial toxins, stimulates or injures the nerve endings, making the infection painful. The infected area is swollen (tumor). Swelling is present because more blood vessels are required to bring more blood into the part; but there is another reason—exudation. Blood cells, plasma, serum, tissue wandering cells, and lymph accumulate in the tissues. When suppuration occurs, the swelling is due also, in part, to pus formation. If the infection is deep or internal, *pain* plus the general symptoms and signs of infection lead to a proper diagnosis and the area involved.

Lastly there is *dysfunction* (*functio laesa*, or disordered function) due to the swelling and pain.

alarming symptoms. They are slower to develop and slower to leave. *Chronic infections*, like tuberculosis, may last over a period of years. They are caused by repeated invasions of organisms rather than by a continued single invasion. *Acute* infections may be become *subacute* or *chronic*.

Infections are further classified according to the type of exudate they engender such as serous, fibrinous, suppurative or purulent, serosanguineous, hemorrhagic, pseudomembranous, or combinations of the foregoing (see Chapter 5). Inflammations (as distinguished from infections) may be produced by any type of injury, physical, chemical, or bacterial. They may be classified as parenchymatous, alterative, or exudative (see Chapter 3); that is, the inflammatory reaction may be due to a degeneration of parenchymatous cells (degenerative) or the production of new cells (alterative, productive, or proliferative) or to the formation of an exudate (exudative).

An acute pyogenic infection gives rise to certain clinical symptoms and signs. First, redness (rubor) is seen if the area is near the skin. An inflamed area is red because of an increased number of open capillaries and a more rapid flow of blood (hyperemia). This may be seen easily in the frog's web. After stroking, a few scattered capillaries are seen; then, with more strokes, new capillaries come into view. Soon the entire field will be full of capillaries and, if stroking is continued, some of the blood vessels will break (rhexis). Severe streptococcic infections may destroy the blood vessels and cause hemorrhage by their lysing effect; staphylococcic infections, although equally or more severe, will not destroy tissue as much because of the reaction which they call forth.

Changes in capillary pressure and in permeability may be caused by variations in *temperature, by tisue activity, and by injuries. Heat produces filtration of fluid* through the capillary wall in one of three ways: (a) by producing capillary dilation, (b) by causing a rise in capillary pressure, (c) by actual injury to the endothelium, resulting in an increased permeability to colloids and a consequent lowering of the effective osmotic pressure. Local injury to the capillaries causes vasodilation, rise in capillary pressure, altered rate of blood flow, and an increase in endothelial permeability with resultant stasis.

Rigdon has studied *capillary permeability in areas of inflammation produced by* xylene. These capillaries show an increase in permeability for about thirty six hours after the local application of xylene. This is indicated by localization in the area of trypan blue, India ink, antitoxins, and vaccine virus. Chemically the skin may show all features of inflammation and yet there may be no localization of the dye. Different irritants affect the capillary permeability more (4 per cent sodium chloride) or less quickly (horse serum). Hyperemia and edema are not determining factors in permeability. *Most bacteria remain within the lumens* of the small blood vessels of the corium when injected intravenously or in the endothelial cells. Staphylococci may reach the extravascular tissues in *areas of inflammation by being phagocytosed by the* polymorphonuclear leucocytes within the blood vessel lumen and then carried through the blood vessel wall. The organism may also adhere or be phagocytosed *by the endothelial* cells severely injuring them, thus allowing the bacteria to penetrate.

Sectioning of the spinal cord has no direct effect on the development of focal inflammatory reaction unless shock is present—then it is retarded. Heparin has no effect on capillary permeability or inflammatory reactions of capillaries or leucocytes.

destruction of tissue whether that destruction follows trauma by mechanical, chemical, or *bacterial agents. Clinically, therefore, pyogenic infection* may end as follows:

1. *Resolution.*—Hyperemia occurs with little or no destruction of tissue. There is early and complete local immunity. The process ends in about twenty-four to forty-eight hours.

2. *Necrosis and Absorption.*—Infection goes a step further. There is some destruction of tissue; the dead tissue is quickly absorbed, and repair is rapid and complete.

3. *Suppuration or Formation of Frank Pus.*—There have been hyperemia and necrosis. The infection was severe enough for suppuration to occur; then immunity is established and repair follows.

4. *Sloughing and Gangrene.*—There is extensive necrosis of tissue due to its destruction by bacterial toxins and interference with the blood supply. *This is seen in streptococcic infections.*

Fibrosis or Scar Formation is the end result of healing in any infection where tissue cells have been destroyed. It is greater after wide destruction of tissue and is especially seen after fungus infections and syphilis.

Calcification is the end result of a tuberculous infection and implies its arrest, but it may follow traumatic injury or other infections (histoplasmosis, coccidioidal) and degenerative changes.

General Effects of Infection.—

Using our previous metaphor, the city at large may also be affected by the burning house (Chapter 3).

In addition to local defenses against bacterial invasion, the resources of the body as a whole are sometimes needed to overcome the invading organisms.

A systemic infection manifests itself through defense reactions. It causes *chills, fever, rapid pulse, leucocytosis, anorexia,* and *general symptoms of malaise.*

In systemic infection fever is helpful because the bodily functions and the forces of immunity work better with an elevated temperature. *It is clearly a defense mechanism.*

Warm-blooded animals (mammals) differ from those that are cold blooded (Pisces, Amphibia, Reptilia) in maintaining a stable temperature, which in man is 98.6° F. This may vary some normally. Often there is a postprandial rise to 99° F. Exceedingly high environmental temperatures prevent heat loss by convection and radiation, allowing regulation only by evaporation. This may cause hyperthermia, as in heatstroke, indicating an overpowering of the heat-regulating mechanism. We shall see in Chapter 11—Water balance, that the body temperature is regulated mainly by evaporation (*70 per cent of the heat is lost in this way during exercise, 25 per cent* normally). Other methods are convection and radiation. This requires sweating and increased circulation to carry blood from the interior to the exterior (where convection and radiation become effective). Therefore, a rapid heart rate and forceful beat are

The clinical symptoms and signs as well as the pathologic changes do not occur in sequence as indicated by this discussion. They occur more or less simultaneously.

The local effects of pyogenic bacterial invasion are accompanied by pus formation. Pus corpuscles are essentially polymorphonuclear leucocytes. They fight bacteria, release an enzyme inhibiting bacterial growth, stimulate the formation of thrombi in lymphatics and capillaries, and make possible the walling-in by a pyogenic membrane.

Bacteriophage.—It is thought by some that in addition to the cells described there is a local agent that aids in annihilating the infective organism. This substance is a protein formed from a precursor originating in the bacteria themselves, for it is formed from cultures grown in vitro as well as in vivo, where its origin is probably more complex. Bacteriophage is a Berkefeld filtrate of bacteria, which, when added to other bacterial cultures converts them usually from "smooth" to "rough," the latter being less virulent except the salmonella and a few other organisms. It seems to engulf them and therefore has been called bacteriophage. D'Herelle thought it was a living organism that destroyed the bacteria. Besredka called it an antivirus (virus against pathogenic bacteria). Other investigators think it a lysate (dissolving bacteria), a chemical substance (local antibody of the bacteria), a colloid suspension (killing by osmosis), an enzyme (digesting bacteria), or a phase in the life cycle of the organism (cyclostage). The exact nature of bacteriophage is unknown. Apparently it cannot be transferred successfully from one individual to another: its action is brief and bacteria will even thrive in its presence after a certain period of time.

A pyogenic infection is one in which the exudate may become purulent—therefore, the name pyogenic or suppurative. It does not always result in the formation of frank pus. Many texts speak of varieties of infections depending on the type of exudate that may occur; namely, serous, fibrinous, serofibrinous, catarrhal, purulent, fibrinous with necrosis of underlying tissue (pseudomembranous), and hemorrhagic. They also include inflammations in this category implying that such exudate may arise from any irritant such as turpentine or aleuronat. It is probably better not to classify infections in this manner because the type of tissue, the time element, the virulence, and amount of antigen and, above all, the resistance of the individual may produce many, if not, all types of exudates in the same tissue during the course of the same infection by the same organism. We have therefore chosen to include under the term pyogenic infection those bacteria which may cause suppuration, and we believe it is better to classify changes which may occur in tissues when the infection is arrested or rather when local immunity is great enough to make the environment unfavorable for bacterial growth and tissue invasion. It should also be said that the terminations of infections are usually given as resolution fibrosis or calcification. The latter are classified here as types of repair following

It is doubtful if injured or traumatized tissue will produce fever. This usually implies infection by a bacterial antigen. Certain protein sensitizations may produce leucocytosis, fever, and even dehiscence of the wound (as in the Arthus phenomenon). However, it is safe to say that postoperative fever is due to infection until proved otherwise. Furthermore, it is probably true that transient bacteriemia is a common sequel to operation in the nose and throat, rectum, kidney, bladder, and all organs normally contaminated. Such bacteriemias are quickly and easily overcome by the average patient.

In infections there is a reduction in heat loss due to vasoconstriction in the skin (causing the patient to appear cold and blue), a reduction in blood volume due to loss of water, and an increase in heat production due to the action of toxins on the heat center. This causes a sensation of chilliness and muscle contractions, which produce more heat. Soon there is an adjustment of heat production and heat loss, the capillaries dilate, and the skin becomes warm, but the whole balance is at a higher level. Barbour suggests the following sequence of events:

The bacterial toxin acts on the peripheral tissues (chiefly muscle) causing catabolic changes. *The catabolic breakdown products increase the affinity of the muscle for* water and cause the withdrawal of abnormal amounts of water from the blood stream. To compensate for the reduction of the volume of circulating fluid, blood is drained from the skin vessels. This makes the skin cold and calls forth a reflex "cold" response from the heat-regulating mechanism. This acts to increase vasoconstriction and hemoconcentration. Finally, the blood becomes warm enough for the nervous system to interpret the temperature as normal or neutral. The chill period has its counterpart in a healthy person by the body reaction to a cold plunge—there is vasoconstriction, diminished heat dissipation, shivering, increased heat production, slight rise in body temperature, blood vessels released from spasm, and stored heat eliminated and skin is warm. The fever period resembles the effects of immersion in hot water with rise in temperature, decreased heat dissipation, and increased heat production as a result of elevation of temperature of the tissue cells (Best and Taylor).

The metabolism in fever brings about changes in water and salt balance—at first anhydremia, later hydremia (this explains scanty urine in the early stages and ample exertion later). Chlorides are retained in the tissues during fever. After fever subsides they are lost in the kidneys and sweat. Tissue destruction is increased and therefore protein may be found in the urine. Carbohydrates spare protein and therefore should be given in fever, since proteins increase kidney work. Carbohydrate metabolism is unaffected and fat metabolism is not disrupted unless there is insufficient carbohydrate to burn the fat.

Fever is not a disease; it is a symptom and indicates that the body is fighting an invading organism. Fever may be absent in overwhelming infections where symptoms of shock prevail. The rectal temperature is about one degree higher than the temperature as ordinarily taken. Food and drink immediately preceding the taking of the temperature by mouth may alter the reading; therefore, the rectal temperature is perhaps more accurate. The pulse follows the rise in temperature, and its quality and rate are of great prognostic import.

There are many clinical types of fever. We speak of remittent, intermittent, and *relapsing types of fever; also of acute and chronic fevers.* The fastigium is the high point of a temperature curve.

1. *Remittent fever* is a fever in which the temperature goes higher in the evening and becomes lower in the morning but does not touch normal. This type is seen in severe general blood stream infections.

necessary. This gives rise to the bounding pulse. The pulse rate increases about ten beats per minute for each degree of fever. The entire mechanism is, according to Cannon, part of the function of the autonomic nervous system designed to produce "homeostasis" in man.

It is probably true that fever results from a decreased heat elimination rather than from an increase in heat production, although the latter does occur with an increase in the velocity of oxidative processes which in turn is due to heat retention.

Moderate increase in body temperature produces no ill effects and has many important functions. Although most textbooks speak of an increased antibody production and function, there is no proof for this statement. In fact (experimental evidence shows that in artificial fever specific antibody formation is inhibited and its destruction accelerated. Fever induced by foreign proteins is beneficial in chronic infections, and malaria has been very helpful in treating paresis. Hyperthermia produced by various electrical devices (short wave diathermy) will kill gonococci and spirochetes but may also cause the death of brain and other tissue cells.

Fever causes: a stimulation of circulation, increased capillary permeability, more phagocytic cells with greater activity to the inflamed area, more food and oxygen to the region of infection, and also more waste and CO_2 carried away from the site. These effects provide for a more rapid neutralization dilution and removal of toxic products which may be eliminated by increased activity of the lungs, kidneys, bowel, and skin.

The mobilization of cells is as important if not more so than the fever. In the treatment of paresis (see Chapter 9), hyperthermia by diathermy is not as effective as by malaria. Nor is the height of the fever as important as its continuation. Its good effects are probably due to the mobilization of macrophage and other types of reticulo-endothelial and lymphocytic cells.

Heat increases blood volume (contraction of spleen, water drawn from tissue spaces) and capillary filtration, and consequently an increase in the amount of lymph and plasma occurs at the atria or foci of infection. This filtration and the increase in blood circulation is made possible also by a reduction in the viscosity of the blood by fever. The work of the heart is thereby reduced. If hemoconcentration occurs and is not rectified, these effects do not ensue.

The explanation for diurnal variations in fever is not definitely known. We have noted that continued hyperthermia may be fatal to cells and to the body. Nature, therefore, gives brief respites more or less completely in intermittent and remittent types of fever. Some explanations for this are the antigen is forced into the circulation and then removed by the reticulo endothelial system; the antigen varies in amount and virulence from day to day; muscular activity during the day causes the rise in the evening which is followed by a fall the next morning due to a night's rest. In general, the intermittent fevers are less serious than the remittent, and a sustained high rise in temperature is usually an ominous sign.

The heat regulating mechanism is under the influence of the central and sympathetic nervous systems and if interfered with by anesthesia or injury, body temperature may be greatly altered. In the premature infant this same influence is manifest. Even in the infant at term external variations in temperature are not stabilized by the body mechanisms because the nervous system does not assume full control over muscles, blood vessels, sweat glands, and other glandular organs for some time. This is especially noted during surgery on young children where hyperthermia may occur easily.

For local and general therapeutic uses of heat, see Chapters 5, 6, 14, and 21.

Fever may be due to infections, to the postoperative absorption of toxic substances liberated by injured tissues (?), to neurogenic causes, as in brain injuries (near the third ventricle), to dehydration (anhydremia), to starvation, to lymphoblastic diseases such as Hodgkin's disease and lymphosarcoma, and to drug action (hypertonic glucose and salt, drastic cathartics, foreign protein, etc.).

It is doubtful if injured or traumatized tissue will produce fever. This usually implies infection by a bacterial antigen. Certain protein sensitizations may produce leucocytosis, fever, and even dehiscence of the wound (as in the Arthus phenomenon). However, it is safe to say that postoperative fever is due to infection until proved other wise. Furthermore, it is probably true that transient bacteriemia is a common sequel to operation in the nose and throat, rectum, kidney, bladder, and all organs normally contaminated. Such bacteriemias are quickly and easily overcome by the average patient.

In infections there is a reduction in heat loss due to vasoconstriction in the skin (causing the patient to appear cold and blue), a reduction in blood volume due to loss of water, and an increase in heat production due to the action of toxins on the heat center. This causes a sensation of chilliness and muscle contractions, which produce more heat. Soon there is an adjustment of heat production and heat loss, the capillaries dilate, and the skin becomes warm, but the whole balance is at a higher level. Barbour suggests the following sequence of events:

The bacterial toxin acts on the peripheral tissues (chiefly muscle) causing catabolic changes. *The catabolic breakdown products increase the affinity of the muscle for water* and cause the withdrawal of abnormal amounts of water from the blood stream To compensate for the reduction of the volume of circulating fluid, blood is drained from the skin vessels. This makes the skin cold and calls forth a reflex "cold" response from the heat-regulating mechanism. This acts to increase vasoconstriction and hemoconcentration. Finally, the blood becomes warm enough for the nervous system to interpret the temperature as normal or neutral. The chill period has its counterpart in a healthy person by the body reaction to a cold plunge—there is vasoconstric*tion, diminished heat dissipation, shivering, increased heat production, slight rise in* body temperature, blood vessels released from spasm, and stored heat eliminated and skin is warm. The fever period resembles the effects of immersion in hot water with rise in temperature, decreased heat dissipation, and increased heat production as a result of elevation of temperature of the tissue cells (Best and Taylor).

The metabolism in fever brings about changes in water and salt balance—at first anhydremia, later hydremia (this explains scanty urine in the early stages and ample exertion later). Chlorides are retained in the tissues during fever. After fever subsides they are lost in the kidneys and sweat. Tissue destruction is increased and therefore protein may be found in the urine. Carbohydrates spare protein and therefore should be given in fever, since proteins increase kidney work. Carbohydrate metabolism is unaffected and fat metabolism is not disrupted unless there is insufficient carbohydrate to burn the fat.

Fever is not a disease; it is a symptom and indicates that the body is fighting an invading organism. Fever may be absent in overwhelming infections where symptoms of shock prevail. The rectal temperature is about one degree higher than the temperature as ordinarily taken. Food and drink immediately preceding the taking of the temperature by mouth may alter the reading; therefore, the rectal temperature is perhaps more accurate. The pulse follows the rise in temperature, and its quality and rate are of great prognostic import.

There are many clinical types of fever We speak of remittent, intermittent, and relapsing *types of fever;* also of acute and chronic fevers. The fastigium is the high point of a temperature curve.

1. *Remittent fever* is a fever in which the temperature goes higher in the evening and becomes lower in the morning but does not touch normal. This type is seen in severe general blood stream infections.

A. B. C. D.

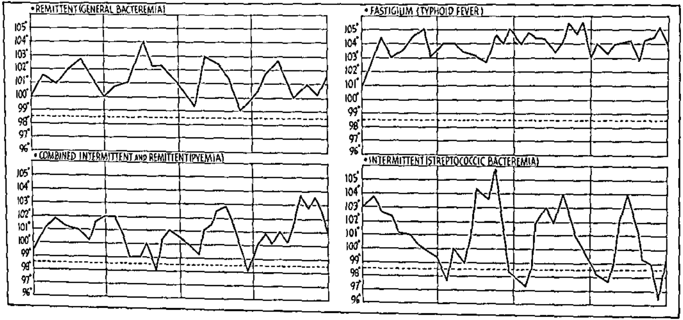

FIG. 24.—Diurnal charts showing types of fever: *A.* Remittent type. The temperature is elevated in the evening and falls in the morning but does not reach normal. (General bacteriemia *due to pneumococcic* empyema thoracis.) *B.* Combined intermittent and remittent type. The curve touches normal or goes below (intermittent type). (Multiple furunculosis with septic embolus in the *kidney on the fourth day.*) *C.* Type showing a fastigium or high plateau during the height of the disease. (Typhoid fever.) *D.* Intermittent type. (Streptococcic bacteriemia due to diffuse cellulitis of the arm.)

2. *Intermittent* fever also shows diurnal variations, but unlike remittent fever, it goes to normal or subnormal and then goes up again (also called "picket fence" type). This type is seen in malaria and in acute infections.

3. The *relapsing* type is seen in the estivo-autumnal type of malaria and in relapsing fever. *The temperature may be remittent or intermittent and then return to* normal for a variable period, only to ascend again.

Various combinations are seen in pyemias, and special types occur in typhoid and pneumonia.

Bacteriemia implies that pathogenic bacteria have successfully invaded the blood stream and its macrophage system. A positive blood culture may show the type of organism. A negative blood culture, however, does not necessarily rule out a bacteriemia. The macrophage system may be full of bacteria which do not live long in the blood plasma. Conversely, the mere presence of bacteria in a blood culture, in the absence of clinical symptoms, does not indicate a bacteriemia in the pathologic sense. Bacteria probably do not multiply in the blood stream unless the reticulo-endothelial system is rendered inactive (experimentally) or is overwhelmed by bacteria. Bacteriemias are therefore transient or intermittent unless the focus, such as a spreading cellulitis, constantly feeds in virulent organisms or there is an intravascular focus (purulent phlebitis, septic thrombophlebitis, pulmonary thrombophlebitis, acute or subacute bacterial endocarditis, or an overwhelming bacteriemia from any cause). Such bacteriemias are sustained. With the use of penicillin it is possible in bacteriemias to obtain sterile cultures from the blood stream and the acute focus. However, unless the focus is drained the septic fever and leucocytosis, which have receded, may soon return. In such cases the bacteria are quickly removed from the blood stream by the reticulo-endothelial system and inhibited by the drugs.

Septicemia is an old term; as usually employed, it includes bacteremia and toxemia (presence of toxins in the blood). The latter is seen in tetanus and diphtheria.

The word toxemia is used very loosely to include states with hypothetical toxins such as the toxemia of burns, intestinal obstruction, eclampsia, and goiter. The toxins of these diseases have not thus far been demonstrated in the blood stream and may be due to a combination of causes; namely, infection, dehydration, hemoconcentration and its effects, anoxemia, and azotemia.

Pyemia means bacterial infection with multiple abscess formation.

Every fever is preceded by a chill.

Hypothermia does not seem to be a compensatory mechanism in infections unless accompanied by shock. (See Chapter 14.) Indeed shock may be associated with a high fever when due to infection. Heat production is due to activity of skeletal muscles chiefly, and, to a lesser extent to glandular action, especially in the liver and kidney. Cold normally stimulates metabolism to increased heat production. This is due to increased production of adrenalin and thyroxin, causing increased tissue oxidation, and to muscular activity. Cutaneous arterioles contract to diminish heat loss and blood is diverted to vital organs (brain, heart, abdominal viscera). Blood pressure may rise. Water is lost from

the blood and diverted to muscles and parenchymatous organs (liver) causing a reduction in blood volume; hemoconcentration may result. Long exposure to cold, according to Wright, may cause a fatigued individual to go into a deep sleep. While in this unconscious state body temperature falls, coma sets in, and death results. A fall in temperature depresses the dissociation of oxyhemoglobin and tends to lower oxidation in the tissue.

Prolonged hypothermia has been artificially induced in patients afflicted with incurable cancer. Here it is said to reduce metabolic activity of cells, slowing up the process of cell division—obviously a temporary accomplishment and not curative.

Experiments on animals with severe infections show that hypothermia does not depress leucocytosis or phagocytosis. Its effect on circulating antibodies has not been ascertained. However, nonlethal pneumococcic infections are changed to lethal pneumococcic infections by lowering body temperature of rabbits to 88° to 90° F. Local chilling of the skin at the site of inoculation inhibited the local inflammatory reaction of the skin.

Crymotherapy or Cryotherapy.—Cold therapy is used in heatstroke and excessively high fever. It may be used locally in certain types of gangrene where amputation is necessary and in sprains to delimit exudation. If cold is used to a degree resulting in refrigeration, it is known as crymotherapy (from *krimo*, icy cold). Cryotherapy (from *krios*, cold) is a milder form of cold. Cold is not indicated locally in the treatment of infections for it lowers oxidation in the tissues when this is undesirable, especially during the period of stasis, q.v. Cold delimits local inflammatory response and decreases oxygen requirements of tissue cells and causes a lowering of their metabolism. It has the same effect on the invading organisms, thereby holding the infection in status quo. Meanwhile the migration of blood and leucocytes has been delayed. *Due to relief from pain, cold is better tolerated than heat and its prolonged use may* cause irreparable damage to cells and capillaries. When the cold is removed, the infection may spread wildly uninhibited. Furthermore, due to local anoxemia anaerobes may grow.

The patient may not realize he is having a chill; he may merely request another blanket. *The exact cause of chill is unknown.* It was formerly thought to be due to blood leaving the periphery of the body. But chills occur when the patient is surrounded by hot water bottles and blankets and when the skin is red and rectal temperature high. In children a chill may be a convulsion. A rigor is a severe and protracted chill. Some believe it to be due to a toxic action on the motor area of the brain. The chill is obviously a mechanism for raising body temperature rapidly; the feeling of warmth, like the sweat after a chill, is part *of the bodily mechanism for rapidly lowering body temperature.* This is reversed in shock, for here the patient feels very warm so that he wants to remain quiet and he sweats—both are physiologic methods for rapidly lowering body temperature. *It is perhaps unwise to interfere with either* mechanism by using cold in the former and heat in the latter. It is also unwise to augment the reactions by using external heat in a chill with a high body temperature or cold in shock with a low body temperature. *If* the patient is able to express his feelings, his comfort should be considered; if not, he should be warmed or not according to his environmental temperature.

The body signal that an infection is present is fever.

Continued fever is usually due to an infection. Such infections may be due to pyogenic bacteria as in subphrenic abscess or other abscesses or to malaria, typhoid, tuberculosis, or syphilis. ***Sometimes the cause is very obscure.***

A patient who has an infection has fever unless (1) it is an overwhelming infection, like a streptococcus septicemia due to septic abortion (where the load of bacteria in the body is too great and the patient is

Fig. 25.—Granuloma at the root of a tooth. The saclike projection is composed of granulation tissue. It is sclerosed at its periphery, forming a connective tissue capsule which *surrounds the cystlike cavity. Such areas are said to be the silent and symptomless* foci of infection. They are probably "tomb stones" marking previous sites of injury or infections which have been successfully overcome.

overcome without any evidence of resistance); (2) the infection is so mild that it is completely localized by the local immunizing forces; (3) the infection occurs in tissue from which absorption does not occur readily (for example, brain) or is present on the surface of the body where the antigen does not accumulate under pressure if drainage is ade-

quate. Fever may occur as a result of protein injection (for example, serum sickness, etc.) and other causes previously discussed. However, when a patient has fever, it should be considered as the result of an infection due to bacteria *until proved otherwise.*

"The fever itself is nature's remedy."

—Sydenham

Changes in the Blood Picture.—The infected patient has also an increase in the number of white blood cells (leucocytosis).

The bone marrow as a hematopoietic organ must be *considered as a unit.* Weltzel showed that in the human adult it has a volume of 1419 c.c., which is thirteen times that of the spleen and almost equal to that of the liver. Since the total amount of tissue *is constant, the proportion of erythropoietic to granulopoietic tissue is consant.* This is about 75 per cent for white and 25 per cent for red cells. Beck states that from three to twenty times more tissue is devoted to the production of granulocytes than to the production of erythrocytes. The volume of granulopoietic tissue is nine and one-half to twelve times that of the spleen. The red blood cell makes about 50 billion round trips and then dies. Bone marrow replaces a trillian erythrocytes each twenty-four hours. These are destroyed and taken up by the reticulo-endothelial system, especially the spleen liberating 25 Gm. of hemoglobin. There are about 100 mg. of iron in 25 Gm. of hemoglobin. Most of the liberated hemoglobin is used over to make new red blood cells. Eighty-five milligrams of iron from old red blood cells is so used each day and 15 mg. is obtained from ingested food—a 100 mg. of iron is a daily requirement.

Blood platelets are present in the ratio of 1 to 20 red blood cells in the circulating blood. They come from the megakaryocytes. They are *increased* after a meal of meat, after hemorrhage, in anaphylaxis, in myeloid leucemia, and after surgery. They are decreased in purpura, aplastic and pernicious anemia, and leucemia.

An increase in white cells is evidence that the "fighting soldiers" are mobilized and ready to repel the invading organisms. Certain conditions are necessary for a leucocytosis to occur:

1. The organism must be of the type calling forth leucocytes.
2. The infection must not be overwhelming.
3. The blood-forming organs (bone marrow) must be normal and able to produce leucocytes.
4. The infected area must be under pressure so that absorption can take place.

Variations in the response will occur depending on the acuteness of the infection and on the kind of tissue that is infected. The vascularity and density of the tissue will affect the absorption and consequently the response. In bone, the response is sudden and pronounced. In the brain no lymphatics are present and absorption is slow due to softness of tissue. Therefore, a brain abscess may occur without fever or leucocytosis.

Walker's index *may be a guide to prognosis.* Ten thousand white blood cells per cubic millimeter may be considered as an average normal blood count; of this number, about 70 per cent are polymorphonuclears.

For every increase of 1 per cent in the polymorphonuclears, there should be an increase of 1,000 in the white cell count. Expressed as a ratio, the normal index (with 10,000 white cells and 70 per cent polymorphonuclears) is 0/0. If the total count is 11,000 and the per cent of polymorphonuclears is 71 per cent, the index is 1/1. In severe streptococcic infections there is a high per cent of polymorphonuclears. If the index is 1 or higher, the prognosis is good; if it is below 1, it is not so good. Say the total count is 30,000 and the polymorphonuclears 84 per cent. This gives an index of 20.14 and a good prognosis. The resistance is high and the virulence low. Repeated counts are necessary in the application of Walker's index. If the sulfonamides have been used, it may not be used accurately. This is not true of penicillin which apparently does not affect hematopoiesis. The Schilling counts are routine laboratory procedures. These also may be distorted by the sulfonamides.

Ponder, Garrey, and others found in normal persons at rest white cell counts of 4,700 to 11,500 and in normal persons during active exercise, counts of 3,500 to 11,500; that is, about the same. Slight normal variations occur also after meals, from nervous or psychic factors, pain, rapid breathing, etc. Perhaps this physiological leucocytosis is due to a vascular readjustment. In general, leucocytes fight infection, are phagocytic, and produce a protease which weakens the antigen. Lymphocytes come later in the course of an infection and aid in the production of antibodies, perhaps macrophages and fibroblasts.

The change in the total number of leucocytes indicates the resistance of the patient; the per cent of polymorphonuclears indicates the virulence of the organism. If the patient has a great resistance the white count should go up.

We have previously seen that at any one time the bone marrow consists of 75 per cent leucocytes and 25 per cent red blood cells, although the total red cell count is much greater. The life of the polymorphonuclear leucocyte is only a few days, for it is constantly being destroyed in its fight against invading organisms. Five to ten billion new cells must be made by the bone marrow each day to make up for this destruction. Red blood cells live thirty to forty days and are destroyed by wear and tear. Lymphocytes are formed in the lymph glands and lymphoid tissue. Lymphocytes live twenty-four hours. Most of them eventually pass into the lumen of the bowel presumably to neutralize the toxins of the intestinal contents by the action of lipase which they contain. They may be related to digestion and stored in the lymphoid follicles and then released. Eosinophiles and lymphocytes disappear from the peripheral circulation of a dog's blood when complete lymphatic obstruction is produced.

Eosinophilia is usually caused by intestinal parasites, trichinosis, arsenic poisoning, eosinophilic leucemia, dermatitis herpetiformes, periarteritis nodosa, Hodgkin's disease, and lymphosarcoma. A variable cause is allergy.

Usually in infections we find a leucocytosis. Other conditions in which high leucocyte counts occur are protein shock, allergy, and intestinal obstruction, especially in mesenteric thrombosis; they also occur after hemorrhage (relative and absolute leucocytosis). Usually, however, a high leucocyte count means infection.

The term *leucopenia* is used to denote a low white cell count.

According to Wright, leucopenia is due to toxic inhibition of bone marrow activity or an increase in the antileucocytic ferment. In the absence of any of the commonly known causes for leucopenia, infection associated with it denotes a poor resistance. It is in such individuals that bacteria may cause extensive sloughing, as in gangrenous stomatitis or spreading gangrene of the abdominal wall. Here the bacteria grow in symbiosis without restriction. It is the "soil" that permits such growth rather than the "seed." An infected, diseased, traumatized, or immature erythrocyte or leucocyte may be quickly removed from the circulation by the reticulo-endothelial or macrophage system. This may account for the swollen lymph nodes and enlarged liver and spleen in many infections, especially those with a leucopenia where, in addition to the removal of inadequate cells, the virus or other antigen must be eliminated.

Lawrence lists the causes of leucopenia as follows:

1. Diminished manufacture of leucocytes by (a) simple inhibition, (b) maturation arrest, (c) aplasia of bone marrow, (d) infiltration of bone marrow with foreign cells.

2. Increased elimination of white blood cells, as in an empyema cavity or through normal channels such as the gastrointestinal tract, lungs, spleen, or liver.

3. Increased rate of destruction in the peripheral blood due to either abnormal white blood cells or to abnormal substances in the blood stream causing their destruction.

4. Redistribution of the white blood cells in the vascular channels such as occurs with foreign proteins.

5. Redistribution of the white blood cells in the body as a whole (leucopenic phase of leucemia).

Granular leucopenia or granulopenia (Haden) is caused usually by (1) a deficient quantity of bone marrow tissue as seen in aplastic anemia, (2) impaired marrow function (aminopyine intoxication produces a qualitative and Banti's disease a quantitative decrease in function, (3) mechanical barrier to the emergence of cells from the bone marrow as in leucopenic myeloid leucemia.

We have frequently encountered leucopenia in a spreading peritonitis. Usually this has been the result of a large amount of semipurulent exudate in the peritoneal cavity. An abscess may precede an agranulocytosis but theoretically it cannot occur when this condition is present because the polymorphonuclear cells are absent. However, a collection of lymphocytes may occur as in empyema of the gall bladder. In typhoid fever with leucopenia osteomyelitis may occur in which frank pus is present.

The sulfonamides may produce impaired marrow function. Therefore, some have advised that these drugs should not be used in the presence of a leucopenia. This cannot be accepted as a general rule. If the leucopenia is due to the bacteria, the drugs may be of inestimable value and the leucopenia may be converted into a leucocytosis. If, however, the drugs cause the leucopenia, they should not be used because it is the leucocytes that annihilate bacteria and not the sulfonamide drugs.

There are certain kinds of infection associated with leucopenia. These may be remembered by the following mnemonic: M_3, T_2, I_2, A. In *measles, mumps,* and *malaria* there is a high fever, but the leucocyte count is low. This is also found in *typhoid, tuberculosis, influenza,* and, at times, in *infectious mononucleosis,* although here there is a lymphocytosis. *Agranulocytosis* is the complete or nearly complete absence of the granular leucocytes from the bone marrow and the blood. It is due to certain drugs and toxic agents as well as to infections.

Red blood counts are important to detect hemoconcentration or hemodilution. Sedimentation rates are increased in widespread infections as in

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as liver and muscle, normally contain anaerobic organisms. They are nonpathogenic unless contaminated by streptococci or other organisms. This explains subcutaneous emphysema (collection of gas) in simple fracture or in contusions where there is no break in the skin and makes us realize that not all infections with gas production are due to the fatal varieties of anaerobes. Some are probably due to gas bacilli and streptococci growing in symbiosis. These are dangerous. Zinc peroxide and the sulfonamides may be used locally. Experiments are conflicting in their results. *This may be due to different types of indigenous organisms in* the animals used. For example, if many streptococci were present in the tissues of the animal they would consume oxygen, producing a favorable environment for the anaerobes. In such cases oxygen through zinc peroxide and bacteriostasis of the streptococcus would inhibit the anaerobes.

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4. *Streptococcus pyogenes* produces diffuse cellulitis, phlegmon, lymphangitis, lymphadenitis, and such distinct entities as Ludwig's *angina, septic abortion, septic band, septic throat*, etc.

In spite of work done by Menkin (see Chapter 5), there is ample evidence that hemolytic streptococci from human hosts rapidly liquefy or dissolve human fibrin. This is not true of streptococci isolated from the cow, horse, rabbit, or guinea pig. Other bacteria tested and found to be fibrinolytically negative were *Streptococcus viridans*, the pneumococcus, *Bacillus typhosus, Bacillus coli, Bacillus dysenteriae*, and the influenza bacillus. Certain strains of staphylococci cause a slight softening of the human plasma clot if the reaction is allowed to continue for eighteen to twenty four hours. Undoubtedly both the fibrinolytic action of the streptococci and the modest tissue reaction they engender play a role in the tendency for the diffuse infections from streptococci to spread.

Infection may invade the entire body through the blood vessels and lymphatics, causing death. It is well to remember the aphorism: "Never enclose a streptococcus in a wound—leave it open," for it is frequently found with anaerobes and can itself exist anaerobically. A wound is better left open if infection is apt to occur. Localization with pus formation may and frequently does occur.

5. *Bacillus coli communis (Escherichia coli)* is an inhabitant of the gastrointestinal tract and may be present in suppurative appendicitis, diverticulitis, etc. It causes dark necrotic sloughs of fascia, has a foul odor, and produces gas in the tissues. It tends to localize ultimately.

6. *The pneumococcus (Diplococcus pneumoniae)* produces pneumonia, pneumococcic peritonitis, and empyema, with pus formation. The exudate is rich in fibrin and therefore the pus is found in large clumps which hang together.

7. *Bacillus typhosus (Eberthella typhosa)* produces typhoid fever. Occasionally it produces suppuration in bone and in parenchymatous organs.

8. *Bacillus pyocyaneus (Pseudomonas aeruginosa)* is a harmless bacterium but it frightens the patient because it forms green pus and has a musty odor. It is a secondary invader.

9. *The gonococcus (Neisseria gonorrhoeae)* produces gonorrhea, salpingo-oophoritis, pelvic peritonitis, suppurative arthritis at times, and even endocarditis.

10. *Anaerobic or gas bacilli* are a group of organisms and include the bacillus of malignant edema *(Clostridium sporogenes)* (the vibron septique) and *Bacillus welchii (Bacillus aerogenes capsulatus*, or *Clostridium perfringens)*. Other members of this group are *Clostridium sordellii; Clostridium septicum norgii; Clostridium sporogenes*, and *Clostridium histolyticum*. They cause gangrene by their toxic action and produce gas in the tissues. Death is due to early septicemia. The *Clostridii welchii* are said to produce three kinds of toxins: hemolysin, dermonecrotic, and lethal. These may be separate or part of the combined effects of toxins and distention of the tissues with gas. Some tissues, such

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Chapter 5

CLINICAL TYPES OF TISSUE RESPONSE TO BACTERIAL INJURY AND CLINICAL TYPES OF SUPPURATIVE INFLAMMATION

Suppurative inflammation is seen clinically in two chief forms, localized and diffuse. *The localized type is usually caused by the staphylococcus,* which incites a vigorous reaction in the tissues. It is this reaction with its blood, cells, fibrin, and plasma which causes the localized variety to remain within the confines of its pyogenic membrane, as we have noted in Chapter 4. The diffuse variety is usually *caused by the streptococcus* which sneaks stealthily into the tissues, and although less virulent than the staphylococcus, it is more apt to spread because the local reaction is weak. This spread gives rise to many complications and sequelae which are not so common in localized types. The exudate offers tangible evidence of the difference in resistance. The former with its destructive onset causes the formation of pus; the latter calls forth a serosanguineous fluid, the result of damaged, dilated, leaky capillaries with very little necrosis at first so that normal tissue architecture is preserved, later to be destroyed.

We must not get the idea that the two types are always and unalterably separate and distinct. It is well known that the staphylococcus may spread wildly due to unusual virulence or lack of local resistance, giving rise to a serious variety of diffuse cellulitis and general bacteriemia. The reverse may be true of the streptococcus which may early form an abscess. Then, too, both varieties may be mixed together, causing a devastating destruction of tissue by their symbiotic activity.

In this chapter we shall first discuss localized infections as exemplified in a form of skin abscess, the boil or furuncle. An abscess is a cavity containing pus. It may occur anywhere in the body. Its clinical manifestations *will depend on the causative organism, the type tissue involved,* and its location. Thus an abscess in loose tissue gives rise to fewer and less severe symptoms than one in dense tissue. Brain abscess, carbuncles, boils, and perinephric abscess may all cause pain, but there may be little or no fever or leucocytosis until the area involved is large and under pressure. Contrast this with osteomyelitis and liver or kidney abscess where there is early and severe pain, high fever, and a great leucocyte response. The pain coupled with the general reaction leads to the diagnosis and the location of the abscess.

We must also consider diffuse types of infection, since both varieties are commonly seen in the hand; a discussion of infections of the hand is pertinent.

THE LOCAL ABSCESS, OR BOIL

By carefully studying the manifestations of a boil, which may be easily observed, we may learn to understand any local infection or abscess anywhere in the body. The normal skin is full of little pits. Some of these permit sweat to pour out (sweat gland ducts); others enclose the roots of hairs (hair follicles), which in turn are lubricated by sebaceous glands (see Chapter 16). Bacteria get into the hair follicle and are usually harmless. Should the follicle or duct become occluded with oil or dirt (comedone or blackhead), the bacteria will grow. Bacterial infection in the follicle destroys cells, calls forth an inflammation, and, as we have seen, the first thing that happens is an increase in the blood supply known as active hyperemia. As a result of this, the hair follicle swells and its opening closes completely. Bacterial growth is increased in this closed, warm, moist space. Microorganisms proliferate rapidly under these conditions. In the last chapter we studied the surgical pathology of inflammation. Let us now compare this with its clinical manifestations, as shown in Table II.

These stages do not necessarily occur separately and in consecutive order. Most of them, as we have already learned, progress more or less at the same time; however, this outline gives us a graphic picture of the progress of localized infections. In addition to these local manifestations, there may be general symptoms and signs. These are chills, fever, leucocytosis, malaise, and anorexia. They vary with the degree of systemic involvement. (See Chapter 4.)

TABLE II

STAGES OF INFECTION

SURGICAL PATHOLOGY	CLINICAL SIGNS AND SYMPTOMS
Hyperemia	Heat (*calor*), redness (*rubor*)
Exudation	Swelling (*tumor*)
Stasis (thrombosis of capillaries and lymphatics)	Beginning of localization
Necrosis (due to bacterial toxins, pressure, and erepsinlike enzymes)	Pain (*dolor*), tenderness
	Pus, sensation of softening; late, fluctuation
Suppuration	Hard area, or wall, around the inflamed zone
Immunity (pyogenic membrane)	"Proud flesh," if excessive
Granulation	New skin
Epithelialization	Scar

The infection starts, then, in a walled-off, closed cavity. Active hyperemia occurs, warning nature of local trouble by chemical and nervous stimuli. Exudation follows. Then the active flow of blood is slowed down (stasis). This permits local plugging of the capillaries and lymphatics by thrombi.

Menkin has shown that phagocytosis is absent at first. The preliminary reaction is one of exudation only. After a few hours granulocytes appear in the wound. These are later replaced by macrophages. This, in part, explains the fallacy of early incision in infections, before "localization" has occurred.

We shall see in Chapter 14 that loss of blood plasma causes the capillaries to become filled with cells. This packing of cells in the capillaries has a twofold action. It prevents reabsorption of the lost plasma so that it may act as an irrigating and diluting fluid and permits local thrombi to form. Certainly this is the cause of stasis in infection. The bacterial toxins render the capillaries more permeable, allowing plasma to exude and thereby limiting reabsorption through the capillaries. Menkin believes that, contrary to popular opinion, the reason for staphylococcic infections remaining localized and streptococcic infections spreading is the extreme reaction created by the staphylococcus. Menkin found that aleuronat and other irritants are fixed in the tissues as a result of mechanical blockade of the lymphatics by intraluminal plugs of leucocytes and coagulated plasma. Trypan blue, when injected into inflamed areas, is retained; in normal areas it is absorbed. With staphylococci, this blockade is established in one hour; with streptococci, it takes forty-five hours (pneumococci, about six hours). The difference in rapidity with which mechanical obstruction is set up may explain the difference in invasive qualities of different bacteria. Staphylococci produce a mild systemic reaction because of their local toxicity; streptococci produce severe general reactions because of their mild local reaction. Menkin's work also explains the good results obtained from prophylactic induction of inflammation in the peritoneal cavity and joints.

We learned in the previous chapter that when either crystalloids or colloids are injected into an experimental abscess after approximately six days, they are not absorbed. These experiments show what happens in a boil or furuncle. Nature closes the tiny capillaries so that the infection will be kept in situ. Sometimes the infection is so virulent or under such terrific pressure that the tiny blood clots are forced out or destroyed. In this event, multiple septic emboli will be carried to distant parts of the body, causing multiple boils or abscesses, *pyemia*, or *septicopyemia*. In the center of the inflamed area the bacteria are destroying tissue (necrosis); should this process of destruction continue, blood clots in capillaries (thrombi) may also be destroyed, with resulting *bacteriemia*.

Nature puts her soldiers (leucocytes and tissue wandering cells) to work. They surround the infected zone until finally local immunity is established. As a result of this battle many dead and living polymorphonuclears are left in the necrotic cavity. These, with cellular debris, lymph, and serum, cause suppuration or the formation of pus. We have spoken of a necrotic cavity. A cavity must have a wall. In a boil this wall is not normal tissue. It is granulation tissue and contains tissue wandering cells, polymorphonuclear leucocytes, lymphocytes, fibroblasts, and endothelial cells. These cells, aided no doubt by humoral antibodies, bring about a local immunity. Furthermore, the closure of the capillaries in the "wall" fortifies the body against the spread of the infection. In other words, there is a living immune barrier to the progress of the infection. On its periphery, capillaries and lymphatics are open, so that fresh blood may be carried to it and debris carried away. This wall of granulation tissue is known as the "pyogenic membrane" or "leucocytic barrier."

Inside the cavity is a "core." The core is made up of necrotic tissue, bacteria, polymorphonuclear cells, fibrin, connective tissue, and cellular debris. The core is in the center because it is surrounded by pus. A solid structure in a liquid medium, with equal pressure on all sides, will work

toward the center by centripetal force. As pus accumulates, it exerts an outward force also (centrifugal); this makes the skin over a boil tense and thin. Because of this pressure and the digestive action of the leucocytic ferments, the skin breaks: the boil has "opened itself." Pus exudes, followed in a few days by the core. The cavity which is left is lined, but not as yet filled, with granulation tissue. Filling gradually takes place and the wound heals by second intention (see Chapter 3). The only difference between this granulation tissue and the kind we find in wounds healing by first intention is that this tissue is filled with immunizing bodies and many more polymorphonuclear cells.

Certain deductions may be made from this study. Trauma, as by squeezing a boil, would break down the "pyogenic membrane." This would not destroy the wall but it would injure it so that the bacteria that were still present would not be held in check. Infection would spread and a second boil would probably develop. One cannot prevent infections from occurring. However, one can bring about early resolutions. The occluded hair follicle should be opened. This is best accomplished by scrubbing the small reddened area with ether, carbon tetrachloride, or grease soap and then washing with alcohol (70 per cent by weight). This will frequently "abort" a boil. Heat aids in localization, especially after the second or third day, because it increases the blood supply to the part. This is done by causing capillary dilatation.

This is not only true on the surface of the body but internally as well. According to Krogh, heat produces a dilatation through sympathetic axon reflex paths as well as through true spinal reflexes. Ruhmann inserted a laparoscope through a small incision and directly observed that the application of heat (46° C.) to the skin of the abdomen brought about a reflex hyperemia of the corresponding part of the intestines in four to six seconds. Bisgard has shown experimentally that heat on the outside of the abdomen slows peristalsis, whereas cold increases it. The reverse is true when hot or cold drinks are ingested. This accounts for the benefits of heat on the abdomen in intra-abdominal inflammations, even though it produces no rise in internal temperature. We have noted that the dilated capillaries in an inflamed area become more permeable, allowing exudation of plasma, and that the exuded plasma cannot be reabsorbed except through the lymphatics. Increasing this dilation allows more plasma and more cells to reach the inflamed area, thus aiding greatly the establishment of local immunity. Cold has the reverse effect, causing constriction of the vessels, slowing of capillary blood flow, increasing capillary permeability through oxygen lack or injury to capillary wall, loss of water into the area, and resulting local anhydremia, thereby increasing stasis and hastening the destruction of tissue.

Brooks and Duncan experimented with temperatures of 10, 40, and 37° C. to determine the effects of heat and cold on wounds. Low temperatures delay the inflammatory response, whereas wounds treated with heat show an accelerated reaction. Both return to the average progress when discontinued. My colleagues and I have experimented with clean and contaminated wounds in guinea pigs and incidentally we observed the effects of heat and cold on wounds. We concluded that cold was not indicated in the treatment of infections even during the first twenty four to forty-eight hours. Cold slows bacterial growth but also the metabolism of cells and their vital blood supply. The most that can be hoped for is a delay in the ultimate reaction. If a part is to be sacrificed as in gangrene of the extremities we are not concerned over the effect of cold on tissue cells nor the possibility of devitalization of such cells. However, in

most instances we are deeply interested in maintaining a viable well-nourished cell even though by so doing we create a more favorable temperature for bacterial growth, for the ultimate destruction of bacteria is by the cell. Since exudation is most prominent during the first twenty-four to forty-eight hours, the important process would be limited by cold. Furthermore, if the sulfonamides or penicillin is given, these drugs cannot reach the area of infection so easily.

Cold used intermittently is followed by vasodilatation. This is an irritating and traumatizing maneuver and should not be used. In all intra-abdominal inflammations cold masks symptoms and produces a delusive improvement.

Pus manifests itself clinically by a central area of softening and late in large superficial abscesses by *fluctuation*. By tapping lightly over the softened center we may elicit a small wave, showing the presence of thick fluid in a closed cavity (also found in incompletely filled cysts and cold abscesses). This, together with the soft center and craterlike edge, assures us of complete localization. Should the surgeon elect to open the furuncle, he will do so through the center. He will then observe the incision to see that it remains open long enough for granulation tissue to fill the cavity. He does not cut through the wall because he knows that this will carry infection into healthy tissue. He does not dare cut away nature's wall of defense. Later he will lift out the loosened core, because it is a foreign body and would delay healing if not removed or extruded by nature.

The treatment of an abscess may be dogmatically stated as follows:

1. Wait for localization. This implies the establishment of local immunity and complete formation of the pyogenic membrane.

2. Provide adequate drainage. This permits "flushing" by pus and avoids pus under pressure.

3. Remove foreign bodies. These prevent free egress of pus and delay repair. In the boil, the "foreign body" is the core. This will usually extrude itself. It should never be torn from its attachment to the granulation tissue.

4. Assure obliteration of the dead space. This is obtained by keeping the wound open so that healing will occur "from the bottom up." Tubes or drains are used for all large abscesses and deep collections of pus. They are foreign bodies deliberately introduced to maintain drainage. They should be avoided whenever feasible, especially in joints and tendon sheaths because, like all foreign bodies, they delay healing, inciting more scar formation.

5. Keep the part at rest. This delimits absorption, prevents injury to surrounding tissue and to the pyogenic membrane, and facilitates repair. Avoid frequent dressings, irrigations, and packings.

6. Give attention to the patient as a whole. Maintain the water balance; give blood transfusion, drugs, etc., if needed.

MULTIPLE BOILS

Sometimes multiple boils will form in a particular area, such as the axilla, the back of the neck, or the scalp. These are due to a decreased

local tissue resistance, such as may be brought about by mechanical friction (collar rubbing the neck), premature incision, or chemical irritation (depilatory, antiperspirant, or deodorant under the arm or strong "tonics" in the scalp). These boils are best treated conservatively; that is, protection with padded bandage and the use of heat. This treatment permits local immunity (local autovaccination) to occur and prevents new "crops" from forming. General furunculosis, such as afflicted the pious and devout Job, is due to *pyemia*. What is known as *Welch's Law of Reciprocal Immunity* is present. If twenty or thirty boils should suddenly occur, the individual would quickly perish. When, however, the boils occur in crops, as they usually do, the patient builds up an immunity to the staphylococcus and the latter, in turn (perhaps because of the slow evolution of the immunity), builds up a resistance to the patient's antibodies—a reciprocal immunity is present. If attention is given to diet, rest, and the general health of the patient, his forces of immunity are usually victorious. *Surgery is seldom indicated* because each boil allows for autovaccination and, as in multiple foci from any bacteria, including tuberculosis, the disturbance of one focus may light up the other. Penicillin and the sulfonamides are extremely valuable. The use of blood transfusions are helpful. Locally, bacitracin is useful.

CARBUNCLE

Due to the anatomical peculiarities of the face, we may speak of carbuncle here as one variety and elsewhere on the body as another. The pathological changes are the same in both.

Body Carbuncle.—For practical purposes we may look upon a carbuncle as a group of boils, joined together by subcutaneous channels. Pus burrows down to the deep fascia along the columnae adiposae of the skin; then it burrows up again, establishing a large indurated area with multiple draining sinuses. Pain is severe and general constitutional symptoms are common. The surgical pathology is the same as that of a boil, multiplied many times as to infected "units." Carbuncle is seen more commonly in patients *without* associated disease, although it is true that in those whose general resistance is low or who have a debilitating disease, such as diabetes or chronic nephritis, the *proportion* who have carbuncles is higher than the incidence in the population as a whole. However, diabetes mellitus, for example, does not per se increase the susceptibility of the person with diabetes appreciably to pyogenic skin infections. It is not necessarily the really sick person who has a carbuncle. It is the one who constantly "picks" skin infections. Women have them on the face more often than men because they molest their faces more. Men have them more often on the neck. In tampering with them these people "make several blades of grass grow where one grew before." Likewise, if the carbuncles are incised too early by the surgeon, infected pus is spread over nonimmune areas, increasing the liability of more infection.

Treatment.—Heat is excellent after stasis has occurred; that is, usually, after two or three days. If used before this time, pain will be more severe, due to overdistention of the already dilated capillaries. We are inclined to do less surgery on boils and carbuncles than formerly. If a carbuncle appears on the arm, it is well to have the patient put the arm at rest in a sling, protect it with a bandage, apply heat, and let it alone. Some surgeons prefer moist heat (that is, hot hypertonic salt solution). Some also use glycerine and magnesium sulfate packs. Solutions must not be used

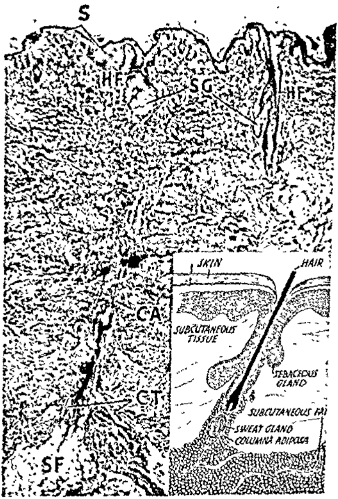

Fig. 26.—Photomicrograph and diagram illustrating the method of invasion of new zones in a carbuncle. The infection descends along the columns of Warren (columna adiposa), following the deep fascia (without invading it), and then ascends along other columns. *S*, skin *HF*, hair follicles; *SG*, sebaceous glands; *CA*, *columna adiposa*; *CT*, connective tissue, *SF*, subcutaneous fat.

continuously because the skin will become macerated. One should use moist packs for thirty minutes, then dry heat for two hours, etc. Carbuncles may be either excised or incised after localization has occurred. Both methods are useful. The latter is preferable in profoundly sick patients. The wound will usually heal without the necessity for skin graft. In either method the pyogenic membrane is not transcended.

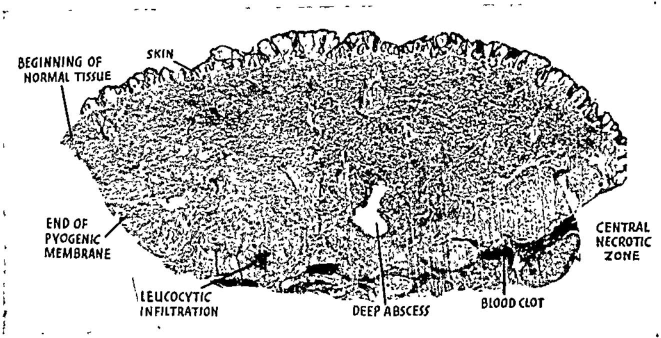

Fig. 27.—Photomicrograph of a carbuncle. On the right is the large central necrotic zone. As the infection spreads, new leucocytic barriers are formed until the entire area is ultimately walled in. (After Berman: Am. J. Surg. 40: 419, 1938.)

Facial Carbuncle.—Carbuncle of the face is a distinct entity because of local anatomical peculiarities. One of these is the blood supply, which communicates through the valveless angular and the superior ophthalmic veins with the cavernous sinus. *Another is the continuation of the platysma* (panniculus carnosus) into the face (as the muscles of expression) without any deep fascia. Since muscle tissue does not easily become infected unless

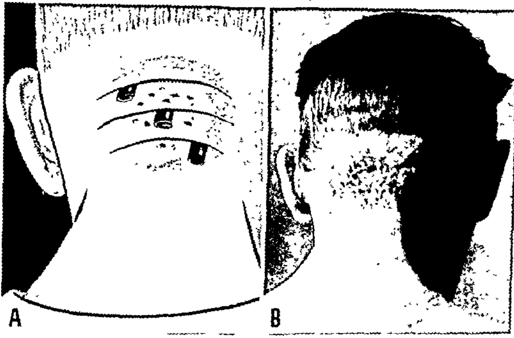

Fig. 28.—Treatment of carbuncle of the neck. *A.* Flaps may be fashioned more safely perhaps by what has come to be known as the "gridiron incision." This is a series of parallel lines with drains inserted beneath the double flaps. In this way each flap has a double blood supply coming from each side. Figure in part taken from Berman, J. K.: Carbuncle, Am. J. Sur., 40: 419-425, 1938.) *B.* Left half of carbuncle has been excised. Right half has been incised, leaving pedicle skin flaps. Note the accelerated healing on the right side due to viable flaps.

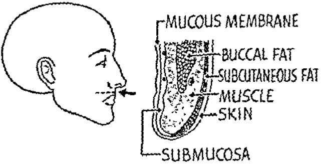

Fig. 29.—Diagram of a cross section of the face at the angle of the mouth. Six layers are shown: (1) skin, (2) fatty layer (traversed by external maxillary artery), (3) buccopharyngeal *fascia*, (4) *buccinator muscle*, (5) *submucous tissue* (*with buccal* glands), (6) *mucous* membrane.

The skin rests on the superficial fascia which is closely intermingled with the facial muscles. The buccal mucous membrane (within the mouth) rests *on* the submucous tissue. The muscles *of* expression are a continuation of the platysma (panniculus carnosus). Infections do *not involve the entire thickness of the cheek unless the muscles are* devitalized. Infection *may* involve the veins (spreading phlebitis) and may be carried by the veins in both directions, owing to the absence of valves.

Due to the laxity of the subcutaneous tissue, collections of *serum* or pus spread easily over the face, causing great swelling. The normal muscles act *as an effective* barrier and rarely do *skin infections involve the mucous membrane*. *The reverse* is also true.

devitalized, an infection in this region spreads laterally, by contiguity. This is especially true of the upper lip and around the nose, the danger zone of the face: septic thrombophlebitis may carry the infection into the brain, causing a fatal meningitis. Not uncommonly a patient will die of *a carbuncle developed by pulling hairs in the nose.*

Treatment.—Treatment should be conservative. X-ray treatment or hot moist packs of hypertonic salt solution may be used. The patient should be at rest in bed. Penicillin and the sulfonamides are given and bacitracin may be used locally. Excision is dangerous (because it may dislodge thrombi and spread the infection); it is also disfiguring. Incision may be necessary but usually is not. Some have advocated tying the angular vein. This does not stop the extension but instead encourages a spreading of the infection in surrounding tissue and in new collaterals that will form. Thrombi would be carried down into the external maxillary vein into the internal jugulars. The trauma of operation may dislodge these.

PARONYCHIA

There are many other examples of localized infections in addition to boils and carbuncles. A common one is *paronychia,* which means "near the nail" or "alongside of the nail" (eponychium). It is characterized by swelling and suppuration near the side of the nail. If it progresses, it may completely surround the base of the nail ("ring around" or "run around"). It results ordinarily from tearing a "hangnail," and though not usually serious, it is very painful and disconcerting. The surgical pathology of this condition is the same as that of other localized infections. The treatment is conservative. A hangnail should not be pulled or bitten off: it should be removed with sterile scissors. Should a paronychia develop, it must be unmolested until suppuration occurs. Then the eponychium is incised close to the nail and the pus evacuated. Too early incision tends to spread the infection. Incision after localization may be made through the thinned skin without anesthesia, painlessly. Soaking the finger in hot saline solution is a common though questionable practice. If overdone, the superficial layers of the skin become macerated. Infected blisters occur which may involve the entire finger. The blister must be opened promptly. If the infection has spread around the base of the nail, it becomes devitalized, acting as a foreign body and delaying healing. The nail should be removed in such cases. Locally, penicillin ointment or bacitracin ointment are beneficial.

Ingrown toenail is a common lesion occurring on the lateral side of the big toe. It is caused by tight shoes and by trimming the nail too short. The soft tissue (vallum unguis or nail wall) is pushed over the nail, which cuts into it, and the result is infection. Prevention consists of cutting the nail long and square, or flattening it with a nail file. Treatment in the early stages is palliative. Cotton, tin foil, or plastic material is introduced between the edges of the nail and the eponychium. In advanced

stages, the lateral edge of the nail and the granulation tissue must be incised. Sometimes the medial side of the nail bed is also involved (double ingrowing nail). The entire nail should be removed but not its root.

FELON

A *felon* is a deep-seated infection occurring in the distal anterior closed space of the finger, frequently involving the periosteum and the bone, with resulting osteomyelitis of the phalanx. It is excruciatingly painful and there is a tense, hyperemic swelling over the palmar side of the finger tip. Early lateral incision is the best treatment. Paradoxically enough, it is unnecessary to wait for localization. The anatomical closed space corresponds to the walled-in area of an abscess, and early drainage must be instituted if interference with the blood supply, because of intense pressure, is to be avoided. Infections in the mediastinum (mediastinitis), the fascial spaces of the neck (Ludwig's angina), and the ischiorectal space (ischiorectal abscess) are also exceptions to the rule, "Wait for localization." Should this occur, necrosis of bone, together with infection (osteomyelitis), will follow. A lateral incision is made, cutting across the connective tissue septa, and drainage is instituted with a small piece of rubber tissue. The finger should be immobilized in a splint. Should osteomyelitis result, sequestration will occur. It is best to wait until the dead bone separates before attempting its removal. Osteomyelitis results in a clubbed finger.

"Collar button" abscess of the palm usually occurs from infection at the site of a callus which has "cracked." This type of abscess usually localizes at the base of the finger after traveling behind the web, through the lumbrical canal, to the back of the hand. Roughly, the abscess resembles a collar button. The treatment is incision and drainage after localization.

DIFFUSE INFECTIONS OF THE HAND

Diffuse suppurative inflammation is usually caused by the streptococcus and has been called phlegmon or diffuse cellulitis.

Every infection of the skin is primarily a cellulitis; that is, an inflammation of cells, with a cellular response.

The dispersing type differs from the localized infections in its tendency to spread along fascial planes and involves veins and lymphatics. There is also more widespread destruction of tissue. Due to lymphatic communication there is a tendency for the infection to invade tendon sheaths, muscle septa, bursae, and joints. The exudate is serosanguineous, not frank pus. It contains relatively few polymorphonuclear leucocytes but has many blood cells. This is said to be due in part to the fibrinolytic and destructive action of the bacteria. Dilated and injured capillaries permit almost whole blood to leak through (although mostly plasma) and not just leucocytes which reach the area by diapedesis and ameboid move-

ment. Due to its widespread involvement there is a great loss of blood plasma, with a tendency for shock to develop. General symptoms are severe and the prognosis is less favorable than in localized infections. An injury, usually small, is followed in twenty-four hours by red streaks on the forearm. Then swellings or "kernels" occur under the arm. The streptococcus has penetrated the skin (first line of defense), invading the lymph vessels and producing a *lymphangitis;* this is followed by invasion and swelling of the axillary lymph glands, or *lymphadenitis* (second line of defense). At this stage there is a dull feeling with malaise. The temperature is 99.5 to 100° F.; there is a leucocytosis, indicating a blood stream invasion. These are the symptoms and signs of a streptococcic infection, with *tubular lymphangitis, lymphadenitis* and *beginning septicemia.*

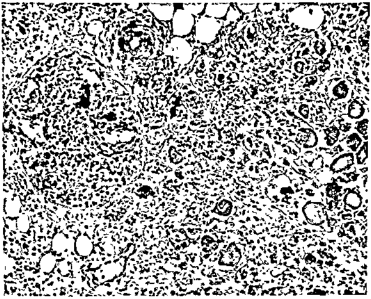

Fig. 30.—Diffuse cellulitis with septic thrombophlebitis. From a case of streptococcic cellulitis of the leg.

Progress and Treatment.—Ninety-five per cent of these patients get well if surgery is withheld. Should an incision be made across the infected tubular lymphatics the bacteria would find easy access to the surrounding tissue. Within seventy-two hours the forearm would be dark red because of a spreading cellulitis and the fever would be septic in type, indicating a general bacteriemia. For this reason it is unwise to cut across infected lymph vessels, *for the lymphatics are better able to cope with the streptococcus than the surrounding tissues.* Should localization with suppuration occur, incision may be indicated. Usually, however, this does not occur. The infection ends by resolution if treated by intermittent hot hypertonic soaks and complete rest and elevation of the arm. Should prompt resolution *not occur, penicillin and the sulfonamides* are used.

Infections of the Hand

If bacteria are *transplanted from one patient to another*, their virulence is increased. Should the surgeon prick or cut his finger, he must *go to the scrub room* and *scrub* his hand for eight minutes "by the clock"; this will encourage free bleeding and will open the wound, sterilizing it. *He must not* put iodine or strong antiseptics on it, for they will irritate the skin and will prematurely seal the wound. All wounds are contaminated but no wound becomes infected until six to eight hours have elapsed, unless a strong antiseptic has been used. Soap and water with scrubbing will remove the transient flora of bacteria in the surrounding skin. Large quantities of isotonic saline are used to irrigate the wound. Price has shown that the transient flora of the skin may contain any number of pathogenic bacteria, the resident flora few. Ordinary commercial soaps are not very good germicides against some bacteria of the skin, especially staphylococci. It is the vigorous scrubbing which mechanically removes the organisms as well as any foreign bodies present. Soap solutions allowed to dry on the skin *do not sterilize the skin surface. Price, in studies on* degerming, has shown that scrubbing the hands with brush, soap, and water *removes the transient flora of bacteria much more readily than the resident* flora. The rate of reduction is by about one-half for each six minutes of *scrubbing. Any antiseptic strong enough to kill bacteria is usually also* strong enough to injure the cells, and it is far better to have healthy cells, *even in the presence of some bacteria, than a temporarily sterile field with* damaged cells. Furthermore, antiseptics quickly lose their bactericidal power when mixed with body fluids, and the injury to cells plus the freshly incubated flora of bacteria under the dried serum actually increases infection. (See Chapter 16.)

Tendon Sheath and Fascial Space Infections

Trauma to the Hand Caused by Human and Animal Teeth.—Usually such trauma is inflicted by a bite but may result from fist-fights or blows on the knuckles in accidents. The most serious is that of the human bite or injury (marsus humanus). The bite of the cat, the camel, and monkey rank next according to Mason. The dog's teeth are clean if he lives in his normal environment and on his normal diet. House pets may harbor organisms in their mouths similar to those harbored by human beings.

The wounds are usually lacerated or contused with devitalization of fascia, ligament, tendon, cartilage, and bone. Tendons may retract, carrying the contaminating organisms deep into the sheaths, or fascial spaces may be directly penetrated. The organisms of the human mouth especially likely to produce a serious infection under such conditions are the nonhemolytic anaerobic streptococci, fusiform bacilli, and spirochetes. Meleney states he has never seen the two latter without the former organism in these infections. Needless to say, there are many other bacteria in the mouth, all of which may have a *synergistic action, thereby increasing their* virulence.

Teeth wounds of the trunk, face, and genitals are less serious. However, in two such wounds of the female breast the results were as severe as in the hand in our experience.

Treatment consists of prompt débridement and scrubbing with soap and water, leaving the wound wide open. Meleney recommends zinc peroxide in a creamy suspension locally. Sulfadiazine given by mouth and penicillin with streptomycin given intramuscularly is good prophylactic treatment. The hand and arm should be immobilized in a splint.

If a streptococcic infection of the hand spreads, it may involve tendon sheaths *(tenosynovitis)* or the fascial spaces of the hand *(facial space infection)*, producing widespread destruction of tissue and resulting in permanent deformity, loss of the arm, or even death. Hand infections require expert care and are treated by bed rest, blood transfusions, sulfanilamide or penicillin, timely incision followed by drainage, external heat, and early mobilization to prevent crippling.

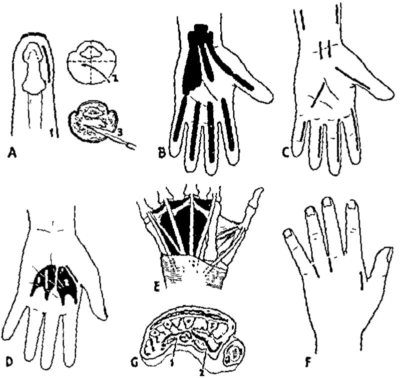

FIG. 31.—Diagrams illustrating anatomic and surgical considerations in hand infections (after Kanavel).

A. (1) The distal anterior closed space. Line shows site of incision. (2) and (3) Cross section of terminal phalanx, showing method of dividing fibrous septa. This avoids compression of digital arteries and subsequent necrosis of bone

B. The flexor tendon sheaths. Note the communication with the radial and ulnar bursae of the first and fifth sheaths, respectively, and the communication between the ulnar and radial bursae

C. Incisions for draining tendon sheaths and radial and ulnar bursae.

D. (1) The middle palmar space. (2) The thenar space. Place for incisions is indicated.

E. The dorsal subaponeurotic space

F. Place for drainage of the above and the thenar space (posterior approach).

G. Cross section of the hand showing the position of (1) the middle palmar space and (2) the thenar space The surgical approach on the palmar side is indicated.

Infections of the Hand

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which is intensified by *extension* of the finger from the protective flexed position. The proper site of incision is illustrated in Fig. 31.

Fascial spaces, as described by Kanavel, are as follows:

1. The *middle palmar space* lies on the interosseous muscles and metacarpal bones, with three extensions into lumbrical canals. This space extends laterally to the middle *metacarpal bone and proximally into the forearm* behind the ulnar bursa. Superficial to it are the flexor tendons, nerves, and vessels, which, in turn, lie beneath the palmar fascia.

2. The *thenar space* lies on the adductor pollicis muscle and adjoins the palmar space on its medial border. Roughly, it occupies the area of the thenar eminence. On dissection it is easy to tear through the delicate partition which separates the above spaces at their superior margin.

3. The *hypothenar spaces* are ill-defined, lying between muscles of this region.

4. The *dorsal subaponeurotic space* lies deep to the extensor tendons upon the posterior surface of the metacarpal bones.

5. The *dorsal subcutaneous space* lies just beneath the skin on the posterior aspect of the hand.

Treatment of Diffuse Infections of the Hand

From this anatomic discussion we may see that the proper management of a hand infection requires exact knowledge of the part and of the clinical manifestations of disease. Modern industry has, perhaps, brought hand injuries to the attention of physicians more than ever. Puncture wounds, compound fractures, and lacerations may be followed by diffuse inflammation. The connections with tendon sheaths have already been mentioned, and the usual association with lymphangitis makes diagnosis and treatment more difficult. The connections between spaces must also be understood, especially the likelihood of thenar space infections to involve the middle palmar space, and the probability of the latter to involve the ulnar bursa, and thence to spread to the radial bursa and down into the thumb. The middle palmar space infection presents a rather typical swelling in the palm and edema on the dorsum because of the fact that the lymphatics take the shortest route to the back of the hand and there is more or less *constriction to lymphatics about the wrist. There are pain and an associated* lymphangitis and lymphadenitis, with fever and leucocytosis. Treatment should be conservative until accurate diagnosis can be made. It is well to stress the possibilities of spread and ultimate crippling of the hand (due to adhesions of tendons and contractures) if there is delay. However, one cannot gainsay the fact that premature incision may have even worse results: it may cause a diffuse or spreading cellulitis involving the entire arm and necessitating amputation of the arm, or it may cause the death of the patient from septicemia. Therefore, if seen within six to eight hours after injury, wounds must be thoroughly scrubbed by the fractional sterilization method (see Chapter 16). Strong antiseptics should not be used. Wounds, depending on the type and age, are closed loosely or left open and covered with sterile gauze and the hand should be immobilized in a splint, over a soft pressure padding. Should infection occur,

Anatomy.—The tendon sheath is a lubricating device composed of two layers, visceral and parietal. The mesotendon is analogous to a mesentery. It is a double layer of synovial membrane and carries the blood supply to the tendon. Tendon sheaths are found only in the hands and feet and around the long tendon of the biceps brachii. The tendon sheaths (or mucous sheaths) of the flexor tendons of the fingers lie immediately subjacent to the skin, the superficial fascia, and the volar digital arteries and nerves. The fibrous sheaths which bind the flexor tendons to the volar surfaces of the phalanges and to the volar accessory ligaments of the metacarpophalangeal and interphalangeal joints cover these sheaths. The sheath of the little finger communicates directly with the ulnar bursa; that of the thumb, with the radial bursa behind the annular ligament (ligamentum carpi transversum). The sheaths of the fore, middle, and the ring fingers extend from the base of the distal phalanges into the palm, immediately proximal to the heads of the metacarpal bones. On either side, at the web, they are in contact with the lumbrical canals containing the lumbrical muscles and digital branches of the arteries and nerves. Since the radial and ulnar bursae communicate, infections may be spread as follows:

From thumb to radial bursa, into forearm, or into ulnar bursa

From index finger into proximal part, then rupture into lumbrical canals, and then into thenar fascial space

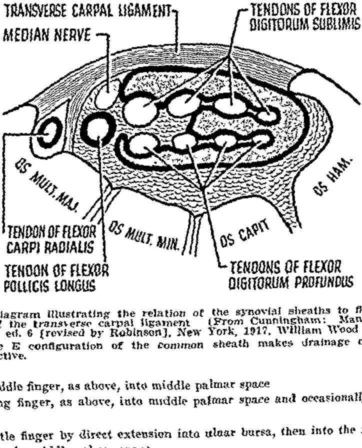

Fig. 32.—Diagram illustrating the relation of the synovial sheaths to flexor tendons at the level of the transverse carpal ligament. (From Cunningham: Manual of Practical Anatomy, ed. 6 [revised by Robinson], New York, 1917, William Wood & Co.)

The reverse E configuration of the common sheath makes drainage on the ulnar side more effective.

From middle finger, as above, into middle palmar space

From ring finger, as above, into middle palmar space and occasionally into ulnar bursa

From little finger by direct extension into ulnar bursa, then into the forearm, the radial bursa, or the middle palmar space

From any flexor sheath of the fingers into the metacarpophalangeal joints.

From radial or ulnar bursa into the wrist joint.

Incision should be made as soon as the diagnosis is made. This is made on the basis of pain or tenderness along the course of the sheath

necessary, and the sulfonamides by mouth and penicillin intramuscularly. Rarely local suppuration occurs; when it does, the area must be drained. In only two diseases involving infections of the lymphatics of the hand and arm do abscesses ordinarily occur along their course; namely, in tularemia and sporotrichosis, the former with lymph node involvement, the latter without. Rarely tuberculosis of the finger or hand may behave in a similar manner.

INJURIES TO THE HAND

Injuries to the hand require prompt treatment not only to prevent infection, but also to repair damaged tendons, nerves, muscles, and skin in an uninfected wound. First aid by factory nurses should consist of the *application of a tight sterile dressing. If necessary, a tourniquet may* be used.

If seen within eight to twelve hours under such preliminary management the wound may be thoroughly scrubbed with soap and water under aseptic technique. Other detergents such as mechanic soaps and carbon tetrachloride may be employed around the wound. These substances should be removed with alcohol, 70 per cent by volume. Ether may be used in *the wound to remove grease. Solid particles are mechanically removed* or picked out of the tissues. A careful débridement is then done. Nerves do not retract and are sutured with fine silk. Tendons do retract. They are brought together with fine silk as described in Chapter 3.

If the injured hand is seen after twenty-four to thirty-six hours or if strong antiseptics have been used, it is perhaps better not to attempt sterilization or primary suture of tendons and nerves. Such wounds are treated as infected and are left open without attempts at primary repair. Secondary suture may be done after five to six days. This may include the tendons and nerves, depending on the degree of contamination. (Chapters 16 and 21).

ERYSIPELAS

Erysipelas may be defined as an inflammation of the reticular lymphatics—a *reticular lymphangitis.* These lymphatics end blindly in the skin *and form a meshwork over the entire body. The disease is caused by* the *Streptococcus erysipelatis.* There are two principal kinds of erysipelas: that which is limited to the face *(facial erysipelas)* and that which is seen in other parts of the body *(cellulocutaneous erysipelas).*

Facial Erysipelas.—Facial erysipelas occurs in old and debilitated patients and in infants. It is characterized by a red zone which spreads across the nose onto both cheeks, assuming the shape of a butterfly. It has a sharp elevated margin (St. Anthony's fire). Locally there are burning and pain on the face. General symptoms are marked, the patient complaining of malaise with chills and fever. It is self-limited and does not involve the eyes but may involve the scalp. It does not form subcutaneous abscesses, due to the absence of deep fascia. *The treatment is supportive and consists*

dry or moist heat, with immobilization and the use of the sulfonamides and penicillin, may stem the tide of the invading organisms.

Careful observation will reveal the space or spaces involved if the foregoing treatment should fail after two or three days. By this time some local immunity has been established so that there is some *anatomical* as well as immunological localization. Under general anesthesia, with the use of tourniquet to ensure a bloodless field, incision is made into the infected space or spaces, and soft Penrose drains are inserted down to the space and not in it. Through-and-through drainage should not be used.

It is unwise to interfere surgically in the presence of lymphangitis, for the tubular lymphatics are better able to cope with the streptococcus than are the loose cellular tissues. The red streaks imply a perilymphangitis as well, and incision allows easy access of the infected lymph to the loose tissues.

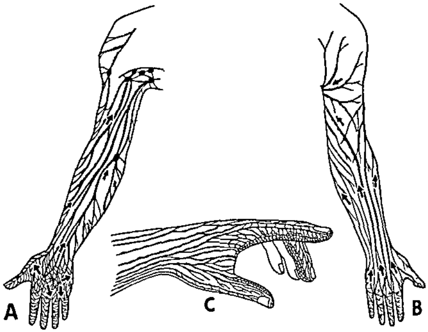

Fig. 33.—Diagram of the lymphatics of hand and arm (after Kanavel and Cunningham). *A.* The anterior surface. *B.* The posterior surface. *C.* The hand. The lymphatics in the hand take the shortest route to the dorsum. Drainage from the ulnar side is into the epitrochlear glands and from them into the axillary glands; from the radial side, directly into the axillary glands. The middle finger may drain directly into the supraclavicular group.

Koch has emphasized Kanavel's teaching of the anatomy of hand lymphatics. They take the shortest course to the back of the hand (which is swollen no matter where the *infection is*), *travel along the flexor surface* of the forearm where those from the ulnar side pass into the epitrochlear nodes, and then reappear and continue into the axillary nodes; those from the *radial side empty directly into* the axillary nodes; those from the forefinger and thumb may empty into the supraclavicular nodes. The treatment is rest to the part by splint (delimiting lymphatic absorption and *allowing* lymphatic plugging, which favors the establishment of local immunity), bed rest of the patient, ample fluid and food, transfusion, if

necessary, and the sulfonamides by mouth and penicillin intramuscularly. Rarely local suppuration occurs; when it does, the area must be drained. *In only two diseases involving infections of the lymphatics of the hand and arm do abscesses ordinarily occur along their course;* namely, in tularemia and sporotrichosis, the former with lymph node involvement, the latter without. *Rarely tuberculosis of the finger or hand may behave in a similar manner.*

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chiefly of sedation, relief of pain, ample fluid intake, and the sulfonamides. Penicillin is efficacious and may be used alone or with the sulfonamides.

Cellulocutaneous Erysipelas.—Cellulocutaneous erysipelas usually enters through a wound and may be anywhere except on the face. It starts in the reticular lymphatics, then spreads down to the fascia by the connecting lymphatics, and is carried along the fascia by the tubular lymphatics. It is not self-limited and tends to spread along the deep fascia, lifting the overlying skin, which may become devitalized. It tends to form local areas of suppuration. General symptoms are marked. The treatment consists of rest or immobilization of the part, hot hypertonic salt packs, incision and drainage over all fluctuant areas as they occur, the sulfonamides internally, and penicillin.

Miscellaneous Varieties of Erysipelas.—*In this group may be included* various clinical types such as (1) migratory, (2) dermatophytid, (3) lymphangitic, (4) recurrent of the lower legs, (5) recurrent varicose vein, eczematoid, and varicose ulcer. Perhaps other clinical varieties may be enumerated which are subdivisions of the foregoing and partake of the same clinical features as well as causative agents.

Migratory erysipelas spreads over various areas of the body in waves. Sometimes all of the cutaneous surface, including the face and scalp, is involved in a succession of episodes. The disease is seen on the lower extremities in association with dermatophytosis of the feet. Some investigators believe that in such cases the inflammation is allergic in nature or a *dermatophytid*. A more reasonable explanation is that the streptococci enter through the fungus lesions, producing erysipelas with or without *lymphangitis*, usually the latter. Sometimes the *recurrent variety of the lower legs* is due to *varicose vein stasis* and *eczema* with minor abrasions or an *ulcer* as the atrium of repeated infection. We have seen patients in whom we could establish no demonstrable cause for the repeated attacks. Even the cellulocutaneous type may be encountered in the legs without apparent cause, although some trauma is probably causative. In all varieties the symptoms may be mild or severe, with chills and fever and high leucocytosis. Sulfanilamide is specific and should be used in doses of 1 to 2 Gm. every four hours until there is a 6 to 8 mg. blood concentration. Penicillin, 50,000 units, every six hours intramuscularly or penicillin in oil, 300,000 units daily, may be employed with or without sulfonamides. In all cases attention must be given to the associated condition.

Erysipeloid is so named because it resembles erysipelas. It is usually seen on the hands of those who handle meat, fish, and cheese, especially in the summer months. Clinically it begins with a small erythematous purplish area which itches. Soon it spreads slowly up the arms. There are few general symptoms. The disease is self-limited. It is thought to be related to a disease in swine (*Erysipelothrix rhusiopathiae*). An immune serum is available and is effective in swine erysipelas and in erysipeloid.

Treatment of Diffuse Inflammations.—This may be briefly summarized as follows:

I. General treatment

1. Rest to the part (in an extremity, splinting)
2. Rest in bed for the patient
3. Sulfanilamide until the concentration in the blood reaches 8 to 10 mg. per 100 c.c. or penicillin, 100,000 units, every three hours intramuscularly until favorable effects are secured
4. Adequate fluid and caloric intake (glucose)
5. Transfusion of blood

The citrate method of blood transfusion is a universal and well-standardized procedure. For technique and quantity employed, see Chapter 13. The amount used in infections will depend upon (a) the patient's ability to take and metabolize food, (b) the rate of blood destruction by the invading organisms as determined by erythrocyte counts and hematocrit, (c) the body's response and its need for more blood, (d) the age and weight of the patient. Plasma may be needed rather than whole blood due to its loss through permeable capillaries and also because of the lack of adequate protein intake and production as well as its excessive loss resulting in hypoproteinemia. It is better to use fresh blood and fresh plasma rather than the stored products because of the higher antibody content in the former (see Chapter 13).

Some observers have advocated the use of immune blood from patients who have recovered recently from like infections and whose blood is full of immune bodies. Others have even advocated the injection of an attenuated antigen into a donor and then later (after six to eight days) using his blood.

II. Local treatment

1. Wait for localization, with abscess formation, before instituting surgery
2. Apply dry heat either by hot pad, water bottle, or heat cradle

The latter is best because it does not traumatize, keeps an equal temperature, provides for moisture (humidifier may be made with a small trough in the cradle), and does not disturb the patient. Recently, cold has been employed in the treatment in infections. This is not good treatment for the reasons given (see Chapters 5, 6, 14, and 20). It is excellent treatment if amputation is indicated as a preliminary preparation.

3. In spreading cellulitis, when necessary as a last resort, amputation may be required.

POSTOPERATIVE INFECTIONS

Postoperative infections are not common after "clean" operations or in uninfected cases. However, with the increasing use of nonabsorbable sutures in surgery, complete asepsis is desirable, for any infection may pro-

duce a long period of disability. The source of the infection may be (1) inadequate masking, (2) upper respiratory infections in the operating team with sneezing and coughing, (3) insufficient scrubbing of hands, (4) breaks in aseptic technique (letting hands down after scrubbing, touching sheets, etc.), (5) contaminated suture material, (6) contamination from bowel or abscess during operation, (7) growth of bacteria in wound during a long operation, (8) the bacteria which are present in all tissues. The prevention lies in eradicating the source, if possible, and in avoiding infection from residual bacteria in the skin, muscle, etc., by the most gentle handling and protection of these tissues. To accomplish this there should be (1) minimal trauma, (2) accurate hemostasis (by the use of small hemostats, accurately applied) in order to prevent blood clots, and necrosis of tissue through taking too large "bites" of tissue (both blood clots and necrosed tissue act as foreign bodies and make excellent culture media), (3) protection of the wound margins by gauze sponges, (4) gentle retraction of the margins of the wound, (5) careful flushing of the wound with physiological saline at the conclusion of the operation, (6) débridement of any fat tissue which may have become devitalized, (7) careful loose approximation of the edges of the wound, and (8) postoperative rest without disturbance of the wound until local immunity has been established (eight days) unless local pain, excessive drainage, or fever demands investigation.

Accidental wounds are discussed in Chapter 16. They should be sterilized and left open or drained.

All potentially infected wounds, such as amputations for gangrene or for spreading cellulitis, should have no flaps (guillotine), and if closed at all should be closed very loosely, with drainage.

Rarely gas gangrene occurs after such amputations. This has been attributed to anaerobic bacteria which are normally present in muscle and which take on growth when it is devitalized. Such bacteria are usually harmless. They are probably made virulent by associated streptococcic infection.

Fever occurring immediately after an operation is due to a mild infection in the wound or at the site of the operation. A rise in temperature occurring after two or three days is also usually due to infection in the wound, although in some cases it may be due to such conditions as phlebitis (femoral, or at the site of operation), thrombophlebitis with pulmonary infarcts, massive collapse of the lung, urinary infections, parotitis, or upper respiratory infections.

A "stitch abscess" is usually caused by the staphylococcus albus. It is not the common type of postoperative infection. The infection extends to the superficial fascia. The patient does not complain of unusual pain. There is no, or very little, rise in temperature. Removal of the stitch supplies drainage and results in early recovery.

After infected cases, such as suppurating appendicitis or spreading peritonitis, the *colon bacillus (Escherichia coli)* may cause a wound infection. There is not much pain but the temperature is elevated. Inspection

of the wound may reveal little. Probing evacuates brown, foul-smelling pus, *which contains air bubbles. Often there is fascial sloughing.* Drainage with removal of sloughs results in recovery, which is often extremely slow. After surgery the colon bacillus may give rise to infections in the abdominal wall which are difficult to diagnose. This is due to the fact that air in a cavity under an incision may be mistaken for a loop of bowel. X-ray examination is of great value. Then aspiration by syringe and needle provide the diagnosis.

Dehiscence of postoperative abdominal wounds should be mentioned here because a diffuse infection in the incision may be the cause. Our experience has been that the infection is only a contributory factor. Delays in wound healing have been adequately discussed in Chapter 3. The factors mentioned apply to postoperative abdominal wounds as well as to others.

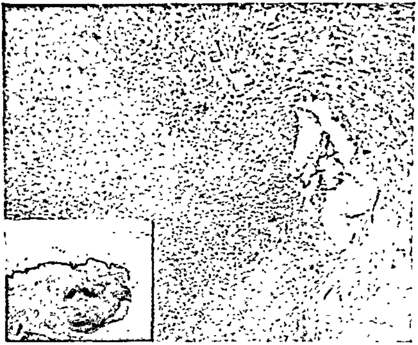

Fig. 34.—Stitch abscess (human). The low power shows reaction occurring about the catgut stitch and the sinus opening in the skin at the point of insertion. The high power shows the stitch (on right), with inflammatory reaction about it. Pus is seen on the upper left.

Usually the separation of a wound is due to a faulty closure (see Chapter 20). There are two outstanding exceptions: incisions which are drained in chemical peritonitis (acute hemorrhagic pancreatitis and perforated peptic ulcer) and operative wounds in very badly debilitated and cachectic patients. In the former, there is actual digestion of sutures (if absorbable) and granulation tissue; infection does not play a part. Therefore, if drainage is indicated, it is done through a "stab" wound. In the latter there is infection but it is usually a secondary factor in an unhealed wound. Adequate pre- and postoperative care may preclude this (see Chapter 2).

Streptococcus pyogenes, especially in combination with *Staphylococcus aureus* (symbiosis), may cause widespread destruction of the abdominal wall. Sometimes gangrene of the abdominal wall results. The cause is the "soil" rather than the "seed"; that is, poor resistance in a very sick patient rather than the unusual character of the bacteria. These infections are often fatal. Free drainage, or "unroofing" of the infected area, is required. Blood transfusions to improve the patient and his resistance are given. Sulfonamides or preferably penicillin may be given, and locally zinc peroxide is useful (Meleney).

Complications of suppurative inflammation include (1) *thrombosis*, (2) *phlebitis* and *thrombophlebitis*, (3) *pulmonary infarction*, (4) *septicemia*, and (5) *toxemia*, and (6) *pyemia*.

Thrombosis, Phlebitis, and Thrombophlebitis.—We have seen that infected thrombi are present in the small capillaries around localizing infections and that although they are usually absorbed, they may be dislodged by the pressure of the accumulating pus and carried by the blood stream to the lungs. In spreading or diffuse inflammations, larger vessels may be involved (thrombophlebitis) and may give rise to emboli. Should this occur in the portal system (pylephlebitis), the emboli would be carried to the liver. In the rectum, either the portal system or the systemic veins may be involved. Infected thrombi are perhaps the greatest hazard of suppurative inflammation. (See Chapter 17.)

Pulmonary Infarction.—The word infarct is derived from *infarcire*, meaning to stuff in. The term has been used to include any tissue destruction from an area of local necrosis to gangrene of the bowel or an extremity. The word was chosen because the collateral vessels about an occluded artery or vein quickly fill with blood and are literally stuffed with red cells. In common parlance it means an interruption of the blood supply of a part with subsequent more or less characteristic changes in the deprived tissues. The obstructed blood vessel may be an artery or a vein. Although it is far more common in the former, the latter is seen in mesenteric thrombosis or a similar state produced by volvulus, strangulation, twisted organ cyst, etc.

The death of tissue is due essentially to a lack of oxygen. Therefore, if the collateral circulation is quickly and adequately formed, infarction may be avoided. If delayed, tissue changes occur even though later, the blood supply with its nutritive material and crystalloids is ample and the waste products are removed.

Karsner believes that infarction in the lung is possible only when there is passive congestion, which may be due to heart disease, other infarcts, pleural effusion, etc., because ordinarily the collateral circulation is so rich that local anoxia is not present long enough to cause the death of cells. It is known, however, that infarcts following pulmonary embolism occur in surgical and medical cases without heart failure (60 per cent), although more commonly in cardiac patients (90 per cent). Perhaps the decrease in vis a tergo caused by the embolus produces its own passive congestion or

the stasis may be a part of the decreased respiratory excursions due to complete bed rest or abdominal distention.

The difference between white and red infarcts is not always due to the type organ involved, that is, white, if the infarction occurs in organs with so-called end arteries, and otherwise red. In dense organs collateral circulation will be less; therefore, the infarct is more apt to be white. Although either white or red infarcts do occur in the spleen or in the lung, both varieties *may be present simultaneously*. *Usually infarcts are white when* they occur in organs with so-called end arteries, as in the kidney, spleen, retina, and basal ganglia of the brain. In organs with a double blood supply infarcts are usually red. This is seen in the lung and liver. The wedge shape which is supposed to be characteristic is due to the fanlike arrangement of the vasculature; this is not always the case.

Abnormal Physiology in Infarction.—Infarcts are not *anemic* if any collaterals are present even though they are *anoxemic*. Therefore, the term anemic infarct should be dropped. Immediately after an embolus there is a peripheral vasospasm although small particles of a thromboembolus may find their way into the arterioles and capillaries of the lung. Then neighboring capillaries dilate (if present) and are stuffed with red cells. Some of these vessels rupture and the area is red. If coagulation necrosis sets in before this rhexis of vessels or if there are few collaterals, the infarct is white.

Anoxemia is the key to the whole local process and causes the death of cells. Coagulation necrosis has been compared by MacCallum to the ruins of Pompeii. The cells, though retaining their outlines, are dead, coagulated intra- and extracellularly. The coagulation is said to be due to a ferment or coagulable fluids from surrounding area and to fibrin.

The sequence of events are therefore local anoxemia, vasospasm, or blockade by small embolic particles, hyperemia (if collaterals are present), loss of plasma, coagulation of cells, cloudy swelling of cells in two hours, and necrosis of parenchymatous cells in forty-eight hours. Connective tissue cells survive longer and may be spared. Dead cells and pigments(decolorization) are removed by macrophages and reticuloendothelial cells. Granulation tissue forms as in any wound. Then healing takes place by second intention with ultimate cicatrization.

If the embolus is infected, a pulmonary abscess may result. Not all pulmonary abscesses are due to septic emboli; some result from aspiration of infected vomitus or mucus during anesthesia. (See Chapter 19.) It is well known, however, that the incidence of pulmonary embolism is as great following local as following general anesthesia, and, according to some, it is three times more common following spinal anesthesia. The reason was thought to be the lowered blood pressure due to dilation of the capillaries and to the longer period of immobility, resulting in stasis in the veins, followed by phlebothrombosis. However, the incidence of pulmonary abscess in such cases is extremely low (Chapter 17).

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which are useful in some chronic infections, although this is open to question (staphylococcic, mixed, tuberculous).

2. Drugs: sulfonamides, penicillin, streptomycin, aureomycin, Choromycetin.

3. Attention to body requirements: oxygen, water balance, blood, and plasma.

4. Physiotherapy (heat) and radiotherapy (early in staphylococcic infections).

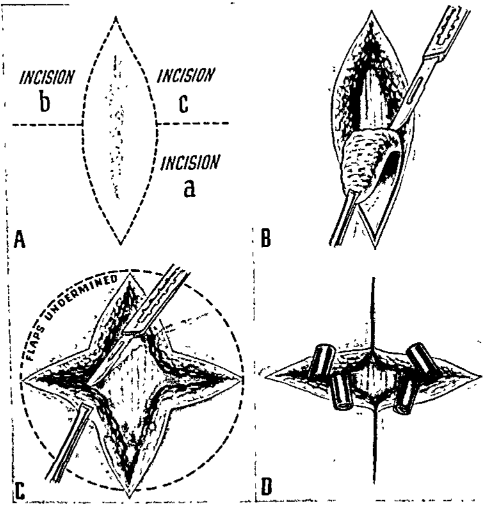

Fig. 35.—Pilonidal sinus. *A.* Lines of excision and incision in the removal of pilonidal sinuses and their ramifications. *B.* Excision of the primary sinuses. *C.* Undermining of flaps and excision of all subcutaneous channels. *D* Partial closure with drainage in infected cases. The wound edges are loosely approximated by subcutaneous absorbable sutures so that subsequent swelling will not produce an ischemia of the suture lines. Other methods of excision are shown in chapter 6 (From Berman, J. K., Am J. Sur. 70: 360-363, 1945.)

Aphorisms.—If the primary focus in an acute septicemia can be eradicated, the patient will probably recover. This is as true of appendicitis as it is of a spreading cellulitis of the hand and arm. In the former, the treatment is appendectomy, in the latter, incision and drainage after

Septicemia (Bacteriemia).—This is a state in which bacteria are found in the blood, a tissue in which they are not normally contained. However, the mere presence of bacteria in the blood stream does not indicate that there is an infection. The bacteria may belong to a strain that is perfectly harmless. If a patient has tetanus or diphtheria, there will be toxins in the blood; this is known as a *toxemia*. The term septicemia is used loosely to include both bacteriemia and toxemia. Formerly the term septicemia was used to indicate the presence of any putrefactive product in the blood; that was before the advent of Pasteur and Lister. A patient with a high fever and repeated negative blood cultures probably has a severe bacterial toxemia. If the blood cultures are positive he is said to have a bacteriemia. A positive blood culture is not invariably obtained when there is a bacteriemia, for the bacteria may be lodged in the reticulo-endothelial cells and the culture may be negative in the presence of severe general infection. The end stage of a bacteriemia will usually yield a positive culture because the reticulo-endothelial system is blocked, humoral immunity is low, and the blood stream is teeming with microorganisms.

Toxemia.—Toxemia has been very loosely applied to mean toxins in the blood from bacteria (tetanus, diphtheria, botulinus, as well as pyogenic organisms), chemical substances introduced (alcohol cyanide), the products of abnormal metabolism (beta-hydroxybutyric and acetoacetic acid), and hypothetical or ill-defined so-called toxins which are present in a great variety of chemical conditions. We speak of thyrotoxicosis in which no toxin has been identified. The toxemia of burns, crush syndrome, intestinal obstruction, and pregnancy may be due to a variety of causes such as dehydration, starvation, hemoconcentration, infection, or anoxemia.

In toxemia of pregnancy such a combination could be causative. If fibrinogen is injected into the portal vein of experimental animals, a patchy necrosis of the liver occurs. This same type of hepatic change is seen at times in severe burns and in the toxemia of pregnancy. In the latter there may be an amniotitis or chorionitis with local loss of fluid into the amnion, producing a polyhydramnios. The continued loss of fluid would cause a hemoconcentration, stagnant anoxemia, patchy necrosis in the brain, kidney, and liver due to the anoxemia, and local thrombus formation. Edema may be due to the leaky capillaries which are made so by anoxemia or to intracellular edema due to the great affinity of tissue cells for sodium for osmotic reasons. The high blood pressure may be a compensatory mechanism to increase kidney filtration. There is no proof for this theory which is given to illustrate what may be the cause of so-called toxemia.

Pyemia.—Pyemia literally means "pus in the blood." Its modern usage implies a septicemia (or bacteriemia) with multiple abscess formation such as seen in multiple furunculosis, multiple osteomyelitis, etc. The treatment of a bacteriemia, toxemia, or pyemia is first the removal of its cause if possible, as will be discussed in the next paragraph. However, there are many important adjuvants which may be used. They are:

1. Biologicals such as antitoxins (tetanus, diphtheria, staphylococcic which neutralizes the exotoxin), toxoids (tetanus, staphylococcic), vaccines

The general ability of a patient to take and metabolize food is a good sign. *It is often the "soil" rather than the "seed" which is at fault.* All laws of prognosis are relative because life itself is relative.

Sequelae of Pyogenic Infection.—

Sinus and Fistula.—A sinus is an abnormal opening in the skin which ends blindly in the tissues and usually discharges purulent material. The most common cause of a sinus is a foreign body; a second common cause is the persistence of an embryonic cavity.

Foreign Bodies.—In children with osteomyelitis where a piece of dead bone (sequestrum) is left, a draining sinus will continue until it is removed or extruded. Because it may act as a foreign body, unabsorbable suture material, such as silk or linen, should not be used in the presence of infections. It is possible for a foreign body to remain in the tissues without sinus formation. If the wound is sterile, or the operation is a clean one, the surgeon may elect to use only silk, as in hernia repair or thyroidectomy. Bullets or pieces of metal may remain in tissues without much reaction and may be completely walled in by fibrous tissue if no infection is present.

Embryonic Cavities.—Pilonidal sinus is perhaps the most common. (*Pilo-* means hair; *nidal* means nest—that is, nest of hair). It is caused by a congenital defect in the gluteal cleft posterior to the rectum. It is lined with epithelium and may extend down to the sacrum. It contains hair and cellular debris and therefore it is caused by embryonic cavity and foreign bodies as well. Since infection is common, it becomes painfully inflamed or it may be discovered because of a local irritation (so-called "jeep disease") excoriation, or abscess. The only treatment is complete eradication.

The branchial clefts should close before birth. Often they remain as small sinuses which are anterior to the sternocleidomastoid muscle in the neck. They become infected and will drain until the epithelium-lined cavity is removed. They may also persist as a fistula or a cyst.

A fistula is an abnormal opening from a hollow viscus to the outside, from one hollow viscus to another, or from a secreting gland to the outside or between blood vessels. (Examples—(1) From a hollow viscus to the outside: complete *fistula in ano* (from the rectum to the perineum); *urinary* fistula (from the urinary bladder to the outside); *fecal* fistula (from the bowel to the outside); *biliary* fistula (gall bladder or common duct to the outside). (2) From one hollow viscus to another: *vesico-intestinal* fistula (a fistula between the bladder and intestine); vesico-uterine (a fistula between the bladder and the uterus); *vesico-vaginal fistula* (this is, in a sense, from one hollow viscus to another and is also from a hollow viscus to the outside) Sometimes the surgeon deliberately makes a fistula to the outside (cholecystostomy, enterostomy) for temporary drainage or from one hollow viscus to another (gastroenterostomy or cholecystogastrostomy) for permanent short-circuiting. (3) Secreting gland to the outside: *salivary* fistula (saliva drains onto the outside of the cheek from the parotid gland due to blockage of the parotid duct or Stensen's duct); sometimes

localization. Should no localization occur in a spreading cellulitis, amputation may be necessary to save the patient's life. Unfortunately the eradication of an acute focus may be impossible. For example, in septic abortion, although the focus is in the uterus, the veins also are infected (thromophlebitis): any attempt at surgical removal would undoubtedly release septic emboli. Therefore, in all cases where the eradication of an acute focus is impossible, the patient should receive blood transfusions, antibiotics, and chemotherapeutic agents, and he should be kept at rest in bed. Later the focus may be eradicated.

A patient who survives the initial onslaught (three to four days) will probably recover.

Fig. 36.—Pilonidal sinus. The low power shows the epithelium-lined sinus and the reaction in the surrounding tissue, the high power shows the hair shafts and the foreign body reaction in the tissue about them.

Patients with jaundice (due to toxic hemolysis, or liver abscess caused by septic pyelephlebitis of the portal system) have a bad prognosis.

Terminal fatalities in pneumonia and in typhoid fever due to septicemia. The consolidated lobe in the former and the enlarged Peyer's patches in the latter are local manifestations of these infections.

The danger of septic emboli is perhaps the greatest hazard in infection. This danger may be partially obviated by rest to the part, prevention of trauma, ample fluid, blood transfusion, and well-timed atraumatic surgery (see Chapter 11).

Every disease with fever should be considered as a toxemia or a bacteriemia and its cause or causes carefully sought. Exceptions are given in Chapter 4.

aseptic, atraumatic surgery in preventing postoperative infections and they do not cure such infections without the aid of proper well-timed surgical management and, above all, the natural response of the body.

First we shall review the general concept of antimicrobic agents and their mode of actions. Then we may list the drugs available, their indications, their contraindications, and their toxic effects.

Practically all antibacterial agents are said to have either a bacteriostatic or bacteriocidal effect. Although it is desirable to annihilate the invading organisms, it is undesirable to injure tissue cells. Bacteriocidal agents are usually antiseptics which are gross protoplasmic poisons. They destroy the metabolic and especially the **catabolic mechanism** of the living cell whether it be bacterial or tissue.

As we have previously avowed, the "age of antiseptics" has joined the age of "boiling oil and hot irons" in the treatment of wounds.

Bacteriostatic agents are the chemotherapeutic drugs. Most of them have a very selective effect on anabolism, catabolism, oxygen consumption ability (sulfonamide), or cellular division (penicillin). Some also have similar effects on certain tissue cells (gramicidin and tyrocidine).

Enzymes (such as lysozyme) act in still another way. They are said to destroy certain structural components of an organism, causing lysis and death, or by digesting away the capsule they may make an organism susceptible to phagocytosis. Thus there have been obtained from saprophytic microorganisms and also from leech extract, enzymes capable of hydrolyzing capsular polysaccharides of pneumococci and streptococci.

Lastly the enzymes may affect end products of bacteria, rendering them toxic for the microorganisms.

Theories as to the Mode of Action of Sulfonamides

There are many theories as to the mode of sulfonamide action. In general it is thought that these drugs produce an environment which is unfavorable for bacterial growth. This is what nature does when she produces a local immunity. The normal protein molecule is not readily utilized by bacteria. They therefore release an enzyme or various enzymes which produce proteolysis. One of the chemical substances which is essential to bacterial nutrition is para-aminobenzoic acid which, in turn, closely resembles the sulfonamide molecule. If, now, a sufficient number of sulfonamide molecules are present, their bacterial enzymes may be prevented from properly engaging the para-aminobenzoic acid and thus be effectively deprived of their nutrition. This is known as competitive enzyme inhibition (Lockwood). If we may use X to denote the bacterial enzyme, then para-aminobenzoic acid plus X equals a metabolite suitable directly or indirectly for bacterial growth. If now we substitute the sulfonamide molecule we have: Sulfonamide plus X equals inactive substance. The law of mass action implies that chemical action is determined by the respective amounts of the substances acting in unit volume or by the degree of the concentrations present. If sulfonamides

combined types of fistula are found. (4) Blood vessels: *arteriovenous* (traumatic or congenital) arterioarterial as in patent ductus arteriosis.

Laws of Fistulae.—If the normal channel is open, the artificial channel will close, unless the fistula is one of the following five types: (1) Tuberculous fistula. (2) Fistula due to a mycotic infection (any disease caused by a fungus). (3) Fistula resulting from malignancy. (4) Purposeful fistula (if a tube is anchored into the intestine, as is done in an enterostomy, the fistula will remain open as long as the tube is in place). (5) Fistula in which the mucous membrane has grown to the skin, or to another organ through disease or surgery. (6) Endothelial lined tubes between blood vessels. For example, if a cholecystostomy is performed, a tube is introduced in the gall bladder to cause bile to drain to the outside. This is a biliary fistula. Now, if this does not heal after the removal of the tube and bile continues to drain, one of five things is at fault: (a) There is a stone or stricture, or occluding pressure on, or in, the common duct, so that the bile cannot get from the common duct into the intestine (normal channel is not open). (b) It is a tuberculous fistula. (c) It is a mycotic infection. (4) It is caused by a malignant growth, such as carcinoma. (5) The mucous membrane of the gall bladder has grown to the skin, forming a mucous membrane lining for the fistula. If the normal channel is open, nature will close the artificial one. This rule is a fundamental one and must be thoroughly understood. Often a patient enters the hospital with an acute intestinal obstruction. He may be too sick for a radical or curative operation. Drainage and decompression are necessary to save life. If the obstruction is in the small bowel, the Levine duodenal or Miller-Abbott tube is introduced through the nose and attached to a suction apparatus (Wangensteen). This usually obviates the need for enterostomy. If the obstruction is in the large bowel, a vent must be made for the escape of gas and feces. Therefore, a cecostomy or colostomy is performed. If the obstructed bowel is released either spontaneously or through further surgery, we need have no concern over a fecal fistula, it will close of its own accord. If the obstruction remains, the fistula will also remain. Nature always uses the normal channel, except for the exceptions noted, thereby permitting the artificial one to close.

THE USE OF ANTIMICROBIAL AGENTS

In this and preceding chapters we have studied in a limited way the great resources of the body to combat infection. We have discussed the cellular, chemical, and mechanical methods employed by nature locally and systemically in fighting pathogenic microorganisms. Although we have indicated forms of therapy it seems fitting that we here review the present status of the newer drugs in combatting infections, particularly the sulfonamides, penicillin, streptomycin, and aureomycin.

It is well to emphasize again that these agents are adjuvants in the treatment of infections. They cannot and do not take the place of careful

Since there is early severe destruction of tissue in staphylococcus infections, the drugs will not be so valuable. In both types late use of the drugs is useful only to attenuate dissemination.

The drugs hold microorganisms in status quo, while tissue resistance combats them. Therefore, the sulfonamides work best in those tissues which have a high local immunity. Because of a good blood supply, there will be less necrosis and the drugs can reach the area. Local cellular response is greater and is given adequate time to mobilize. The diluting action on toxins of serous fluids, normal serum, or lymph is important. They are not antisulfonamide as is pus.

Pharmacology

The pharmacologic activity of the sulfonamides depends upon solubility, absorption, excretion and acetylation. It is these factors which determine the type drugs to be used. However, toxicity, idiosyncrasies and rate of elimination are also important. The point to remember is that sulfonamides are not specific for specific types of antigens. They are specific in the fact that they are in great local concentration because of one or the other factors mentioned. The acetylated forms of the drugs are therapeutically useless. Sulfadiazine, for example, is the least toxic, is readily absorbed, is rapidly excreted, and is therefore very useful in hemolytic streptococcic, pneumococcic, and staphylococcic infections. Succinylsulfathiazole (sulfasuxidine) and phthalylsulfathiazole (sulfathaladine) are useful in preparing the large intestine for surgery because they cause a lowering of the numbers of coliform bacteria in the bowel. These drugs practically remain in the large intestine (Poth) and have a very low coefficient of absorbability.

Local Use.—Much has been written about the local uses of the drug. Such factors as solubility, absorbability, chemical reaction of the wound, and antisulfonamide factors are all important. One cannot be dogmatic about its use at this time. However, certain factors must be considered. If the action of the drug is bacteriostatic, then its introduction into the infected area has no effect on surface bacteria. It must be absorbed and find its way into the tissues. The only reason then for its local use would be a quick and high local concentration. For this reason it would have to be used in fresh wounds or early in infections when absorption takes place, before antisulfonamide factors are present and before capillaries and lymphatics are blocked. Thus the drug is useless locally in an abscess, a badly macerated wound, or a late infection. Another important factor is the effect of the drugs on tissues. They are not rapidly absorbed and many are irritating. An irritative foreign body is certainly not desirable, especially in serous cavities. Since the drugs are not germicides, they must be sterilized before being used Some have advocated their local use after débridement. If débridement is indicated, infection has not yet occurred and the drug will probably reach the site as quickly and more universally given systemically because antisulfonamide factors have been removed

are present in greater amount than any of the so-called antisulfonamide factors (para-aminobenzoic acid, peptone substances, bacterial extracts, animal tissue and co-enzyme, also vitamin B complex, of which para-aminobenzoic acid is a part, local anesthetic agents of the procaine series), then bacteriostasis will occur. Although many other theories have been used to explain sulfonamide action (peptone theory—Lockwood, 1938, peroxide-catalase theory—Mellon and associates, 1938), the foregoing is perhaps most useful as applied by Stamp, 1939, and Wood, 1940.

Recently still another theory has been advanced. Henry states that other inhibitors of the sulfonamides are certain purines, amino acids, glucose, mercuric chloride, and urethrane. If the theory that metabolites like para-aminobenzoic acid are inhibitors, then some of these substances should not be. He believes that the sulfonamides act on bacteria like narcotics, especially in inhibiting the relatively small amount of total respiration needed for supplying energy in cell division.

Certain changes are observed in the capillaries as a result of treatment with sulfonamides as well as with other drugs such as the iodides (see chapter on glands, thyroid). Perivascular infiltration may cover a wide area around a vessel. Such changes may occur from the use of the sulfonamides, a process not unrelated to periarteritis nodosa. In acute diffuse infections the capillaries are open and permeable. After sulfonamide therapy they soon become blocked with fibrinous plugs. A streptococcic cellulitis becomes converted into a localized lesion, permitting surgical drainage. This is certainly not entirely due to the inhibition of bacterial growth. It may be due in part to an effect on blood lymph capillaries. This is further substantiated by the bizarre types of localization in empyema, peritonitis, cellulitis, and other types of generalized infections. Although there is no proof for these conclusions, clinical observations tend to substantiate them. Probably no one theory explains their actions—perhaps a combination of effects is produced.

Whatever the mode of action, it is apparent that an early large amount of sulfonamide concentration is desirable at the site of infection so that antisulfonamide factors will not have time to form and also so that early capillary occlusion will occur. The drugs are not bacteriocidal; if they were, a continuous supply would have to be available at all times until bacteria were annihilated. They are bacteriostatic for a limited period, allowing the forces of local immunity to combat microorganisms. This immunity is apparently not prevented or delayed by the drugs. The fewer proteolytic substances in a wound, the less competition for the sulfonamides and the better they will behave. It follows that the drug will work best where local reaction is least. Fortunately for the surgeon, then, the type of surgical infection which is helped most is the type in which early surgery is contraindicated. Another way of putting it is: the less damaged the architecture of the part, the more easily will the drug reach it and therefore the more effective it will be. The reverse is also true. Thus early in streptococcus infection the sulfonamides are very useful to invite localization.

individuals although they be mixed together in one compound. In other words, the compounds retain their individual solubility. They are said to have a low risk of renal injury and a negligible incidence of crystalluria, and therefore alkalies and fluids are not as important as in the sulfonamides previously employed alone. There is also a low degree of acetylation. For example, a saturated aqueous solution or urinary solution of sulfadiazine can still be fully saturated with sulfamerazine and still further saturated with sulfamethazine. Furthermore, the effectiveness of the compounds is said to be greater when used in combination than when used singly. The *drugs are put out in the form of a tablet or in a suspension. One brand* of triple sulfonamide mixtures is known as Terfonyl (Squibb). The tablets contain 0.167 Gm. each of sulfadiazine, sulfamerazine, and Sulfamethazine (0.5 Gm. of sulfonamides). The suspension contains 0.167 Gm. each of sulfadiazine, sulfamerazine, and Sulfamethazine per 5 c.c. of suspension (0.5 Gm. of sulfonamides per teaspoonful).

Sulfonamides are also used to reduce the coliform flora of bacteria in the *large intestine. Sulfasuxidine is absorbed very slowly and may* be used as follows for preoperative bowel preparation: 0.25 Gm. per kilogram of body weight divided in four doses per twenty-four hours at six-hour intervals. The tablets are 0.5 Gm. each. Other indications for the drug are ulcerative colitis and regional enteritis. In these diseases it is given in one-half the above dosage. Sulfathaladine (phthalylsulfathiazole) is said to be less toxic than Sulfasuxidine and may be used in smaller doses; for example, as *an adjunct to surgery* it may be given in the dose of 0.1 Gm. per kilogram of body weight. The tablets come in 0.5 Gm. size. In ulcerative colitis and regional enteritis a smaller dose is used—usually about .05 Gm. per kilogram up to 0.1 Gm. per kilogram per day.

Closely related drugs, the sulfones (Diasone, Promin and Promizole), are being used with encouraging results in the treatment of leprosy. Still a newer type of sulfonamide is Thalamyd (Schering) which is phthalylsulfacetimide. This drug is said to have antibacterial action for enteric organisms such as *Escherichia coli, Shigella dysenteriae, Shigella paradysenteriae, Streptococcus faecalis,* and *Vibrio cholerae.* The drug is used in ulcerative colitis and also in the preoperative sterilization of the intestines. The dose is 0.2 Gm. per kilogram of body weight in twenty-four hours. Usually 4 to 6 Gm. per day suffice for adults with ulcerative colitis but larger doses are used before surgery and in acute dysentery.

All drugs which destroy or inhibit the growth of coliform organisms in the large intestine may interfere with the formation of vitamin K_2 and therefore this vitamin is given daily as long as the drugs are employed.

Toxic Effects.—Almost every type of reaction has been observed. The more common ones are:

1. Effects on blood and blood vessels (agranulocytosis, acute hemolytic anemia, aplastic anemia, methemoglobinemia, purpura hemorrhagica, thrombocytopenic purpura)

and the blood supply improved. In potentially infected or infected wounds where drainage is used or the wound is left open, the drugs may be safely employed. However, they are lost in great measure with the exudate. If the local principles of wound healing are adhered to and if infections are treated according to sound surgical principles, there will be no need for the local use of the drugs. If they are violated, the drugs cannot be relied upon to perform the miracles which have been erroneously attributed to them.

Indications and Contraindications.—Throughout the book mention will be made of specific clinical indications. In using the drug there may be a sensitization of the individual which may prevent their future use and bacteria may become immune in such persons, rendering the drug useless. Therefore, these compounds should be used only where definitely indicated.

Names of Drugs.—There are many varieties which are in use. Some are still in the experimental stage. For individual variations the student is referred to a text on pharmacology and therapeutics. The original sulfanilamide is the least irritating and most valuable locally. It is effective though more toxic than other compounds. The others can only be mentioned. They are sulfapyridine, sulfadiazine, sulfaguanidine, phthalylsulfathiazole (Sulfathaladine), succinylsulfathiazole (Sulfasuxidine) sulfamerazine, and Sulfamylon.

Dose and Mode of Administration.—The sulfonamides are usually given by mouth with adequate alkalinization to minimize crystalluria. When oral administration is not possible, soluble salts may be administered intravenously (5 Gm. as an initial dose and then 3 Gm. of a 1 per cent solution three times a day) by rectum or vagina. Absorption takes place from wounds and even the intact skin. Only sterilized powder should be used intravenously in solution. Doses are extremely variable. Sulfanilimide is given to adults in initial doses of 1 Gm. per 9 kilograms (20 pounds) of body weight and repeated in twenty-four hours in six doses. Maintenance dose is 10 Gm. (150 grains) every twenty-four hours until a blood level of 10 to 15 mg. per cent is reached. Another method of oral administration is to give 4 Gm. as an initial dose and then 1.0 to 1.5 Gm. every four hours. In either case equal amounts of sodium bicarbonate should be given and liberal amounts of water consumed. After the temperature has been normal for twenty-four hours the dose may be cut in half. For children up to 12 years a proportionately greater dose may be employed because fluid intake per kilogram is great. Sixty milligrams (1 grain) per pound is a good initial dose. This may be followed by an equal amount every twenty-four hours in divided doses.

Since sulfadiazine is less toxic, it may be used in larger doses and may be given intravenously. Orally 4 to 6 Gm. may be given as an initial dose and then 1.5 Gm. four times a day. Effective blood concentration is 8 to 15 mg. per cent. Parenterally 5 Gm. may be used intravenously and then 3 Gm. of a 1 per cent solution three times a day. Recently sulfonamides have been used in mixtures. The triple sulfonamides are found to act as

which will enable the physician to give a type of penicillin which is rapidly absorbed but which will be excreted rapidly or penicillin which is slowly absorbed.

Sodium penicillin or crystalline sodium penicillin G is a preparation which is extremely soluble and may be dissolved in small amounts of sterile distilled water or sterile isotonic salt solution or 5 per cent dextrose solution. The dose for intravenous injection is 10,000 to 50,000 units per cubic centimeter of sterile isotonic solution of sodium chloride. Usually it is given along with intravenous solutions for the maintenance of water balance; 100,000 to 200,000 units are given with each injection. For constant intravenous drip, 25 to 50 *units per cubic centimeter of sterile saline solution* or 5 per cent glucose solution should be given. For intramuscular injection, 50,000 units per cubic centimeter of isotonic solution of sodium chloride should be given or 100,000 units in 2 c.c. By giving the solution intramuscularly the concentration may be more sustained and the blood levels will remain comparatively high.

Preparations of penicillin are now available which prevent rapid absorption. At first an ice bag was applied to the area of injection to produce vasoconstriction and, therefore, to slow the rate of absorption. At present, there are many preparations available which will accomplish this end without the use of vasoconstricting agents. Crysticillin (Squibb) is a *brand of procaine penicillin G for aqueous injection.* This is absorbed slowly and an initial dose of 300,000 units may be given intramuscularly dissolved in 1.2 c.c. of sterile distilled water or sterile isotonic sodium chloride solution. This will be absorbed over a long period because it has a low water solubility. *Another preparation for delayed action is* Depo-penicillin (Upjohn). There are 300,000 units per cubic centimeter. This is a crystalline procaine penicillin G suspended in peanut oil and containing 2 per cent w/v of aluminum monostearate. This, also, is slowly absorbed. Still another is Duracillin (Lilly) which is a crystalline procaine penicillin G in sesame oil. Penicillin S-R (Parke-Davis) represents a combination of procaine penicillin G with buffered crystalline sodium penicillin G. The rationale for the use of this combination is that the procaine penicillin G will be absorbed slowly whereas the sodium penicillin G will be absorbed very rapidly, the mixture giving an immediate effect and then a prolonged or sustained effect. In the acute pneumococcic, staphylococcic, or streptococcic infections, 400,000 units, that is 1 c.c. of the preparation, may be given daily and continued daily for at least forty-eight hours after the temperature has returned to normal. When indicated in severe infections dosages as high as 800,000 units may be employed twice daily. This, then, represents a combination of penicillin, which is absorbed quickly and which has an absorption that is extremely slow. All of the "fortified" products have the advantage of prolonged action so that continuous intravenous injection of the drug or intramuscular injection every three hours may be avoided. However, it is felt by many observers that *since the rate* of absorbability does vary, that to be safe in severe infection, it is, perhaps,

2. Skin (dermatitis exfoliativa), other types of dermatitis, cyanosis
3. Gastrointestinal (vomiting, nausea, diarrhea)
4. Urinary tract (azotemia due to urinary obstructions from crystalluria or renal insufficiency or sulfonamide mud in Bowman's capsule
5. Liver (hepatitis, toxic necrosis, blue jaundice may be hemolytic or intrahepatic)
6. Central nervous system (dizziness, tinnitis, psychosis, and convulsions
7. Fever

These manifestations may occur from comparatively small doses in sensitive individuals, whereas while most of these reactions are in themselves harmless, they emphasize the importance of using the drugs only where definitely indicated because such reactions occur more commonly in patients having had the drugs. Furthermore, they *contraindicate to a* greater or lesser extent their continued use.

Antibiotics

Penicillin.—Penicillin is derived from a mold, *Penicillium notatum*. Alexander Fleming of St. Mary's Hospital, London, first described it in 1929. It was not until the stress of war casualties became acute that the possibilities of this drug were really explored. This was principally through the efforts of Chain and Florey in 1940.

Action.—The exact way in which penicillin inhibits bacterial growth is not known. However, it appears that the drug does not interrupt the growth of bacteria but prevents cellular division in vitro and in vivo with the frequent production of giant forms. It appears to have an antiendotoxin action also. It is fairly well known, however, that it does not affect animal cells either in their growth or metabolism. It may be said then that its toxicity is extremely low. However, it may have a direct toxic and primary irritant effect, perhaps due to impurities, especially when used intrathecally. It may also have antigenic properties (erythema, hives, angioneurotic edema, dizziness, epistaxis, etc.) or therapeutic shock excitant effects (Jarisch-Herxheimer), producing convulsions. Indirect effects are also listed; namely, too rapid healing of a coronary or liver lesion may have deleterious effects on these organs.

It is effective in all staphylococcic infections with and without bacteriemia, all cases of clostridial infections, all hemolytic streptococcic infections locally and with bacteriemia, all anaerobic streptococcic infections, all pneumococcic infections, all gonococcic and meningococcic infections, and also gram-positive bacilli and spirochetal infections. It is ineffective against gram-negative and acid-fast bacilli.

Dosage and Administration.—Since penicillin is rapidly excreted in the urine (two to four hours), a continuous supply should be available. It may be given orally, by continuous intravenous, or by subcutaneous or intramuscular injection. Various preparations of penicillin are available

thricin concentrate to be diluted to 1,000 c.c. These solutions always contain 0.5 mg. of tyrothricin per cubic centimeter.

Streptothricin.—Streptothricin is a bactericidal substance from a soil Streptothrix *(Actinomyces lavendulae).* It prevents the growth of *Escherichia coli* and other gram-negative bacteria. It also has an antibiotic action against numerous fungi and yeasts. In the experimental animal it is toxic in large doses. Robinson suggests that this product may be useful in the treatment of bacillary dysentery and typhoid and colon infections. It may therefore supplement penicillin which is not effective against gram-negative infection. As yet it is still in the experimental stage.

Streptomycin.—Streptomycin is an antibiotic derived from a strain of *Actinomyces griseus.* It is used clinically as streptomycin hydrochloride and streptomycin sulfate and is particularly useful in the treatment of gram-negative bacilli infections. It may be given intramuscularly, subcutaneously, intrathecally, intrapleurally, and intraperitoneally. Very little is absorbed from the gastrointestinal tract, but it is useful orally in doses of 1 Gm. every six hours to reduce the number of coliform bacteria in the colon. The average dose for intramuscular use is 1 to 2 Gm. daily in divided doses at six-hour intervals for 7-14 days. In children under 2 years of age up to 0.4 Gm. may be given daily. It is frequently given with penicillin and may be mixed in the same syringe, avoiding separate injections. Streptomycin has been most effective in the treatment of tularemia, *Hemophilus influenzae* infections, urinary tract infections due to gram-negative bacilli, bacteriemias and meningitis due to gram-negative infections, and peritonitis due to colon bacillus and in conjunction wth penicillin in all types of peritonitis and tuberculosis. Toxic effects include histamine-like reactions, headache, vertigo, and eighth nerve deafness when given in very large doses, neurological disturbances, paresthesias, hypersensitive reactions, fever, skin eruptions, and eosinophilia. After about two weeks its effectiveness is greatly reduced.

Dihydrostreptomycin.—Dihydrostreptomycin is the dihydro derivative of streptomycin A which is pure streptomycin. Mannosidostreptomycin (streptomycin B) also has a dihydro derivative (dihydromannosidostreptomycin). These antibiotics produced in the laboratory from streptomycin are said to be less toxic and may therefore be given for a longer period of time. Streptomycin and dihydrostreptomycin are used in the treatment of tuberculosis in a daily dosage of 1 Gm. up to forty-two days of treatment; 0.5 Gm. is given intramuscularly every twelve hours. With this dosage there is less likelihood for toxic reactions. Also in the smaller dosage the development of a resistant strain of tubercle bacilli making it impossible to employ streptomycin in the future is not apt to arise. Dosage of more than 1 Gm. may be followed by more toxic reactions involving the eighth nerve without increasing the therapeutic response. Extending the treatment beyond forty-two days results in greater clinical response, but there is the danger of developing a resistant strain of bacteria. The

best to rely upon an injection of the soluble form of penicillin or crystalline sodium penicillin G so that one will be sure of its absorbability. This is given every six hours in the dosage required which is usually 100,000 to 300,000 units as the indications demand. The toxic effects of all of the penicillin products which are fortified, so to speak, and which prevent rapid absorption are not great and many products have very low toxic action. The patients who are allergic to penicillin or to procaine may develop hives or angioneurotic edema. Such patients may be treated effectively by the antihistamine drugs.

Penicillin may be used locally in solution or soluble jellies or as a powder. It has some local irritating effects and although it is not readily absorbed in this way, sensitizations do occur. It is therefore profitable to give it intramuscularly as well as locally should such treatment be indicated.

Here again emphasis should be placed on the fact that the drug is an adjuvant to surgical treatment. For example, we treated a large number of patients with empyema thoraces by thoracentesis and injection of the empyema cavity with sodium penicillin C. This sterilized the cavity readily but, as we have seen, such cavities usually must be drained to permit proper wound healing. We found, therefore, that the cavities filled with purulent exudates over and over again with recurrence of fever. Only after surgical drainage did healing occur. Likewise a gross violation of surgical technique will not be mitigated by penicillin. Perhaps when used early some cures may result from penicillin alone.

Gramicidin and Tyrocidine.—Gramicidin and tyrocidine are produced in cultures of *Bacillus brevis* (a gram-positive aerobic spore-forming soil organism). Tyrothricin consists of both gramicidin and tyrocidine.

Action.—These substances are effective against gram-positive organisms, although gonococci and meningococci are somewhat susceptible. *Gramicidin* is toxic for erythrocytes and spermatozoa also. Its action is said to be due at least in part to inhibition of the bacterial enzymatic action and retardation of growth, causing lysis of susceptible bacteria. *Tyrocidine* is toxic not only for bacteria, but also for all types of living cells. It is therefore like an antiseptic in that it completely and irreversibly inhibits cellular metabolism. Therefore it is not suitable for either local or systemic use.

Dosage and Use.—*Tyrothricin* is used in solutions for *local use only.* Even its introduction in body cavities with adequate drainage is not free from danger. Its chief use thus far has been in indolent superficial ulcers. Tyrothricin concentrate (Sharp & Dohme) is supplied when diluted to make an isotonic solution which contains 0.5 mg. of tyrothricin per cubic centimeter. Three dosage forms are available: one is a 1 c.c. ampule containing a solution of tyrothricin, 25 mg. per cubic centimeter. This is diluted to 50 c.c. of sterile distilled water; the second is a vial containing 10 c.c. of tyrothricin concentrate to be diluted to 500 c.c. with sterile distilled water; the third, for large quantities, is a 20 c.c. ampule of tyro-

fections, bacillary urinary infections, rickettsial diseases, and lymphopathia venereum. The drug is given by mouth in doses of 50 mg. per kilogram of body weight. The dose varies from 3 to 6 Gm. the first day and 2 to 3 Gm. thereafter. Toxic effects are slight. Chloromycetin is obtained in sealed capsules containing 0.25 mg. each.

The great variety of drugs which are now available and which are being developed afford the physician a choice of therapy in so-called "resistant" infections. Thus in penicillin-resistant infection, Chloromycetin may be useful, etc. Also various combinations of drugs are extremely beneficial because few infections are due entirely to one strain of organism.

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average daily dose for children is about 7 mg. per pound of body weight; that is, approximately 15 mg. per kilogram of body weight.

Aureomycin.—Aureomycin is an antibiotic derived from a strain of *Streptomyces aureofaciens.* It has been used in rickettsial diseases (Q fever, Rocky Mountain spotted fever, murine typhus, and rickettsial pox) brucellosis, typhoid fever, and urinary infections caused by the coli-aerogenes group and *Streptococcus faecalis.* Aureomycin hydrochloride is given orally (0.25 Gm. capsules in doses of 0.75 to 1 Gm. every six hours. This dosage maintains a constant serum level of 2 to 6 mg. per milliliter. The drug diffuses into most body fluids and tissues, including the cerebrospinal fluid. The use of aureomycin against virus diseases, buboes (Ducrey's bacillus), and streptococcal and staphylococcal infections is also encouraging. Aureomycin may be used in smaller dosage for less virulent infections; 25 mg. per kilogram of body weight every twenty-four hours divided into four equal doses or 500 mg. every six hours for average adults is a desirable way to give the drug. The full dosage should be continued for one to two days after the temperature has returned to normal. Aureomycin hydrochloride may be given parenterally, 1 c.c. for each 10 mg. of aureomycin. The diluent is leucine, 2.6 per cent solution. The dose is approximately one-fifth that of the oral dosage. Intravenous use is more apt to be followed by reactions. Nausea and vomiting are frequent upon oral administration, and after intravenous administration thrombophlebitis may occur.

Bacitracin.—Bacitracin was isolated from *Bacillus subtilis* and is a diffusible polypeptide of low molecular weight. It resembles penicillin in its activity against gram-positive bacteria and spirochetes. Bacitracin is excreted by glomerular filtration, and blood levels are maintained for five to ten hours. The drug is most useful as a topical application for various infections (100 to 200 units per cubic centimeter of physiological saline). It may be given intramuscularly but has little effect orally. Also local injection around boils (500 units per c.c.) using 0.1 to 0.5 c.c. has been advocated. Toxic effects are chiefly on the kidneys; however, this may be due to impurities.

Subtilin, Subtenolin, and Bacillomycin.—These are all derivatives of *Bacillus subtilis* and show promise of being helpful in tuberculosis, typhoid, and fungus infections, respectively.

Polymyxin.—Polymyxin has been isolated from the soil organism *Bacillus polymyxa.* Given intramuscularly in divided doses of 0.2 to 0.5 Gm. daily, usually about 3 mg. per kilogram of body weight, the drug is said to be useful in the treatment of brucellosis, pneumonia, and typhoid fever. It has serious nephrotoxic properties and is therefore still in the experimental stage.

Chloromycetin.—Chloromycetin comes from a species of streptomyces *(venezuelae)* and contains nonionic chlorine. It can be prepared synthetically. It is used in the treatment of typhoid fever, typhus, salmonella in-

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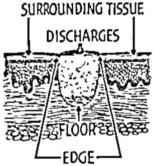
The following classification is based on etiology:

A. Direct injury to the part
   1. Trauma to tissues (severe crushing force)
   2. Prolonged pressure
      a. Decubitus ulcer
      b. Splints
      c. Volkmann's ischemic contracture
      d. Crush syndrome
   3. Thermal injury
      a. Heat burns and scalds
      b. Electrical burns
      c. Radium and x ray burns
      d. Cold (frostbite)
      e. Immersion foot



EDGE	RAISED,	INFLAMMATION OR NEW GROWTH
	OVERHANGING,	SYPHILIS AND TUBERCULOSIS
	ROUND,	NEUROPATHIC ULCER
	UNEVEN,	NEW GROWTH, SYPHILIS, ETC.
FLOOR	FIBROSED, GRANULATION TISSUE	OLD
	RED AND BLEEDING	NEW
	ELEVATED,	EXCESSIVE GRANULATION
	LEVEL	HEALING
	UNDERMINED,	ACTIVE DESTRUCTION, (FUNGUS, ELECTRICAL BURNS)
SURROUNDING TISSUE	EDEMA AND CYANOSIS,	VASCULAR DISEASE
	NO CHANGE,	NEUROPATHIC
DISCHARGES	SEROSANGUINEOUS,	PASSIVE CONGESTION, (VARICOSE ULCER)
	THICK,	STAPHYLOCOCCUS
	THIN,	STREPTOCOCCUS

Fig. 37—Ulcers. Diagram indicating some of the more important clinical characteristics and their possible significance. The site of the ulcer is also important, as for example; lower lip—syphilis or carcinoma; inner side of lower leg—varicose ulcer; outer side of upper leg—syphilitic ulcer; sole of foot—neuropathic ulcer, etc. Biopsy, smears, and general examination are always indicated to make or confirm the diagnosis.

Chapter 6

ULCER AND GANGRENE—WOUNDS WHICH DO NOT HEAL ACCORDING TO THE NORMAL LAWS OF REPAIR

An ulcer is a sore or a solution of continuity of the surface. It is a defect in which healing does not occur according to the normal laws of repair or in which repair has been delayed. Much can be learned by careful clinical study of the ulcer. (1) The *edge*, if raised, may mean the presence of active infection or new growth; if overhanging, it indicates that some active process, such as syphilis, is destroying the granulations but sparing the skin. (2) The *floor*, if covered with red granulations, indicates that the ulcer is acute; if pale and fibrosed, it indicates that the ulcer is old. (3) If the *surrounding tissue* shows venous stasis, there will be no healing. (4) The *secretions*, if purulent, indicate a pyogenic infection; if serosanguineous, a streptococcic infection or simply a passive congestion, as in varicose ulcer. (5) *Position*. An ulcer on the lower lip indicates squamous-cell or prickle-cell carcinoma; on the cheek, basal-cell carcinoma or rodent ulcer; on the upper outer leg, syphilis. Although in a given disease the position is not invariable, the sites which have been described are characteristic. Thus an ulcer differs from a wound which is healing by second intention in a normal manner. For in the latter, granulation tissue fills the defect and then the skin or mucous membrane grows across it. Diagnosis is made by a careful history, general and local physical examination, and laboratory tests including serology, smears, and biopsy from the ulcer.

Gangrene is the death of a part. The term *gangrene* is usually used to imply the death of a large area, such as an extremity, whereas *necrosis* generally refers to the death of a smaller area of tissue. Some authors use the term gangrene to mean necrosis with invasion of saprophytic organisms—wet gangrene. This type is seen peripherally in some cases and usually when internal viscera are involved. The dry variety is described then as infarction due to vascular causes or as ischemic necrosis.

A classification of ulcers and gangrene may be based on a number of different criteria: (1) clinical manifestations, (2) etiological factors, and (3) pathological changes, according to the disease process that is present.

The following classification is based on etiology:

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     c. Volkmann's ischemic contracture
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     a. Heat burns and scalds
     b. Electrical burns
     c. Radium and x ray burns
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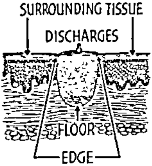
     e. Immersion foot



EDGE	RAISED	INFLAMMATION OR NEW GROWTH
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	ROUND	NEUROPATHIC ULCER
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Fig. 37.—Ulcers. Diagram indicating some of the more important clinical characteristics and their possible significance. The site of the ulcer is also important, as for example; lower lip—syphilis or carcinoma; inner side of lower leg—varicose ulcer; outer side of upper leg—syphilitic ulcer; sole of foot—neuropathic ulcer, etc. Biopsy, smears, and general examination are always indicated to make or confirm the diagnosis.

4. Chemical
   a. Strong acids and alkalies
   b. Weak acids (carbolic, lysol, etc.)
   c. Injection of drugs (superficial gangrene)
      (1) Neoarsphenamine
      (2) Adrenalin
      (3) Ergot (local or general)

B. Indirect injury due to circulatory disorders
1. Venous congestion
   a. Varicose veins
2. Arterial causes
   a. Functional
      (1) Vasodilatory—erythromelalgia
      (2) Vasospastic—Raynaud's disease
      (3) Combination—Sudeck's post traumatic dystrophy of the extremities
   b. Organic causes of gangrene
      (1) Arteriosclerosis (senile)
      (2) Diabetes
      (3) Embolism (in acute infections, in sepsis, postoperatively, etc.)
      (4) Thromboangiitis obliterans; Buerger's disease
3. Lymphedema
   Ulcers may occur due to interference with superficial circulation of blood

C. Gangrene of infectious origin
1. Gas gangrene
2. Phlegmon or diffuse cellulitis
3. Hospital gangrene (phagedena or wound diphtheria)
4. Noma (gangrenous stomatitis); Hunner's ulcer of the urinary bladder
5. Ulcers due to specific bacteria or virus
   a. Tuberculosis
   b. Syphilis
   c. Mycotic infections
   d. Chancroid
   e. Lymphogranuloma inguinale
   f. Granuloma inguinale
6. Leprosy

D. Neuropathic ulcers
1. Mal perforant
2. Corneal ulcer (after trigeminal nerve operation)
3. Peptic ulcer (?)

E. Malignant ulcer
1. Basocellular
2. Marjolin's ulcer (old burned area)
3. Spinocellular

F. Ulcers associated with splenomegaly
1. Sickle-cell anemia
2. Splenic neutropenia
3. Banti's syndrome
4. Hemolytic (spherocytic-acholuric) jaundice

G. Disturbances of fat metabolism

1. Local fat necrosis (lipogranuloma) of breast and abdominal wall
2. Lipophage granulomas (Darier sarcoid; erythema induratum, Bazin's disease—may be tuberculids or tuberculosis in fat)
3. Relapsing febrile, nodular, nonsuppurative panniculitis or Weber-Christian's disease—etiology is unknown
4. Necrobiosis lipoidica diabeticorum

H. Combinations

1. Ulcer of tongue in syphilis
2. Leprosy and neuropathic causes

DIRECT INJURY TO THE PART

Trauma to Tissues

Trauma to the tissue caused by severe crushing force needs no examples. It simply devitalizes the tissue so extensively that sloughing occurs and the remaining devitalized tissue is slow to heal.

Fig. 38.—Decubitus ulcer. Case of myelitis.

Prolonged Pressure

Decubitus Ulcer.—Decubitus ulcer (bed sore) is usually seen in old people and in those who are debilitated or have been in bed for a long time. This lesion occurs on the posterior parts of the body that are in constant contact with the bed—the sacrum, the heels, the shoulder blades; also over the trochanters and ilia. By far the most common place is over the sacrum, for here there is direct pressure of skin against bone, which interferes with the blood supply, and moisture (due to soiling or per-

spiration), which causes maceration in a potentially infected area. These sores can be prevented by changing the patient's position frequently and by keeping him clean and dry. Should any signs of redness or blister occur, an ulcer may easily result. This is practically always followed by infection. After an ulcer has formed, the treatment is to relieve pressure (by a rubber ring or by having the patient lie in a prone position) and to keep the part clean and dry. Antiseptics play a minor role; however, there is no objection to the use of mild ones, such as boric acid or one-half per cent Chlorazene. Normal salt solution is probably just as effective. Some use stimulative ointments, such as scarlet red salve; pectin-agar acid mixtures have been used with good results. A far better plan of treatment is to wait for granulation of the ulcer bed and then slide full-thickness adjacent flaps into place after excising the devitalized margins of the ulcer. In paraplegic patients this may be done with excellent results. In others it should be attempted only after improvement of the general condition of the patient. In aged and debilitated patients the closure may be done in stages, or split-thickness grafts may be used.

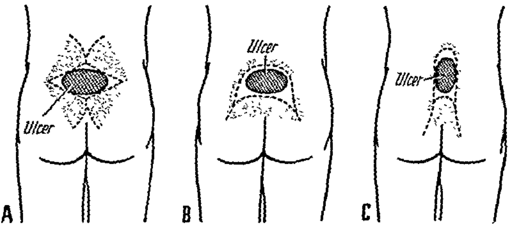

Fig. 39.—Treatment of decubitus ulcers. Formerly the treatment of decubitus ulcers and of pilonidal cysts and sinuses was excision of the diseased tissues and then a long period of waiting until the healthy granulations appeared. After this occurred, skin grafts were applied, usually of the split-thickness free graft type. It is now known that with proper attention to the general condition of the patient and with adequate mobilization of flaps that pilonidal sinuses and decubitus ulcers may be excised and closed primarily. *A*, *B*, and *C* are a few examples of this procedure. Obviously the type of excision will vary, depending upon the position and configuration of the ulcer. In every instance it will be noted that adequate mobilization of flaps must be secured and that suture lines must not be under tension. Then with firm pressure dressings, wounds will heal provided the general condition of the patient has been properly cared for.

Splints.—When splints are applied too tight, there is constant pressure, which devitalizes the skin. Therefore, there should always be a heavy padding around the splints to avoid pressure, especially over bony prominences. Plaster casts carefully applied need very little padding.

Volkmann's Ischemic Contracture.—This is a horrible complication resulting from venous obstruction, with asphyxia of the tissues and their subsequent destruction. This is followed by extensive cicatrization of muscle, tendon, and fascia, with permanent deformity and crippling of the part. It is usually seen after fractures of the elbow that have been

immobilized in acute flexion or in tight casts which interfere with the venous return, although the same process has been described in the foot following fractures in the knee. (See Chapter 21.)

Hemorrhage and edema in the antecubital space may so interfere with venous return as to cause a Volkmann's contracture even though no splints have been used. The increase of hydrostatic pressure in the veins causes a loss of blood plasma, with actual rupture of the veins and hemorrhage. Although the arteries are not occluded, the obstruction causes a rise in venous pressure equal to the systolic pressure in the capillaries and arterioles; all circulation ceases and death of the tissue follows. There is evidence to show that a sufficient collateral venous circulation exists normally in the elbow region. Horwitz believes there is interference with the arterial circulation by direct occlusion. This, of course, may be true in some cases. Usually, however, the radial pulse is normal or only slightly weakened.

If there are pain, swelling, and cyanosis in an extremity, the danger of Volkmann's contracture is imminent. Treatment consists in immediate removal of the cast or splint, extension of the arm, and, in some cases, multiple incisions in the edematous area to relieve pressure. Once necrosis has occurred, the arm and hand will atrophy and the latter will assume a characteristic deformity known as "claw hand." This illustrates the importance of close observation of a fractured extremity.

Wringer injuries are produced by the compression which the rollers exert on the hand, forearm, and arm. This injury is followed by extreme swelling along the entire arm. The pathological effects may be destruction of muscle and tendon due to direct trauma or indirectly due to interference with circulation as in Volkmann's contracture. Children are usually the victims. The treatment should include a pressure bandage applied over liberal wads of mechanics' waste equally distributed; also, elevation of the arm. Repeated injections of physiological saline solution subcutaneously has been used by us with good results. Incisions in the antecubital space may be necessary to relieve pressure, which is especially apt to occlude venous return in this area. The application of cold has been advocated by some.

Needless to say, all electric wringers should be equipped with an automatic cut-off device.

Crush Syndrome.—This will be discussed in Chapter 14 under shock. Severe injuries to the extremities during World War II were common in England, especially in civilians who were crushed under falling buildings. If the legs were severely compressed, the patients exhibited all of the symptoms of shock when compression was removed. By standard treatments such individuals responded for several days only to die with a second group of symptoms resembling uremia and accompanied by anuria. Tourniquets should not be used in such extremities. Local treatment consists of pressure bandage or subcutaneous physiological saline infusions. In addition, plasma and all of the remedies mentioned under burns are indicated.

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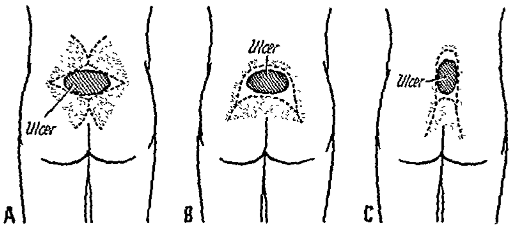

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A *third degree* burn destroys the stratum germinativum, becomes infected, and usually requires grafting. But even here the epithelial cells around the hair follicles may minimize scarring.

It is not the depth of the burn that determines the prognosis but the extent of the burn. In other words, the patient may have an entire arm burned off with less serious results than a second degree burn that covers one-half of the body surface, for this may prove fatal. It should be said, however, that a third degree burn involving a similar area would be even worse, not only because of shock, but also due to toxemia, infection, and the difficulty involved in securing autogenous grafts to cover the area. Usually in extensive burns all degrees may be present in different sites simultaneously. It is difficult to ascertain the degree of the burn until the slough occurs.

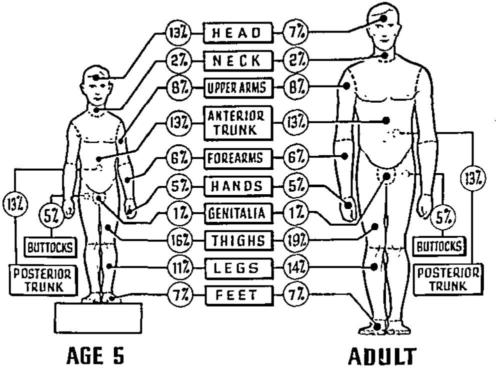

Fig. 41.—Diagram of estimated surface areas of burns. The percentages are based upon figures from Lund and Browder Surg., Gynec. & Obst. 79: 352, 1944.)

The surface area involved is usually calculated according to Berkow's formula: Head, 6 per cent; trunk, 38 per cent (anterior surface, 20 per cent; posterior, 18 per cent); upper extremities, 18 per cent; lower extremities, 38 per cent. For children of all ages trunk and upper extremities are the same but for the head 10 per cent is added for each year the age is below 12 and the same amount is subtracted from the lower extremities.

A very accurate table has been constructed recently by Lund and Browder and is presented herewith (Table III).

It is important to know the surface area involved for accurate recording, prognosis, and treatment.

Thermal Injury

Heat Burns and Scalds.—*Burns* refer to thermal injuries by dry heat; *scalds*, to injuries by moist heat. Chemical and electrical burns will be discussed under separate headings. It is perhaps true that more children die of burns than of diphtreria and scarlet fever together.

Surgical Pathology of Burns.—There are three *degrees* of burns, first, second, and third. The epidermis is composed of four layers: the outer layer is known as the stratum corneum; then come the stratum lucidum, stratum granulosum, and, lastly, the stratum germinativum, or Malpighian layer. This innermost layer is important because it is the one that makes the new cells. Beneath this is the dermis, which is composed of the stratum papillare and the stratum reticulare. Old textbooks described six or seven degrees of burns, depending on how deep they were, the last degree connoting complete destruction of the part, including bone. Such burns are seen in extremities. We now speak of only three kinds in extensive burns because survival does not occur in deeper varieties.

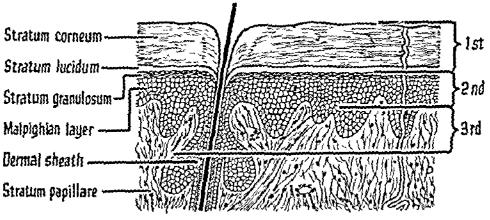

Fig. 40.—Diagram illustrating degrees of burns. The first degree burn involves the *stratum corneum* and may include the *stratum lucidum* and *stratum granulosum*. As a rule, it does not become infected and leaves no scar. The second degree burn involves the *stratum germinativum* (Malpighian layer) in part. There is usually no infection and the skin is mottled, with some areas of scarring. The third degree burn goes deeper, involving the corium (*stratum papillare* and *stratum reticulare*). There is infection and scarring, but even here some islands of epithelium may be seen, arising from the dermal sheath surrounding the hair. A fourth degree burn would involve the *entire skin* and *stratum subcutaneum*. Extensive burns are usually of mixed second and third degree type and require skin grafting to prevent vicious scarring.

A *first degree* burn does not leave a scar. This means that it has not destroyed the stratum germinativum and will not become infected. Since the outer layers (strata corneum, lucidum, and granulosum) of the skin are partially intact, blisters will form in first and second degree burns. It is perhaps the stratum corneum which is most important in retaining fluids which have escaped from peripheral blood vessels.

A *second degree* burn leaves a scar, but not an unsightly one, because it penetrates part of the Malpighian layer but not all of it. The skin will be pitted (pig skin) after healing is complete. Grafting will be unnecessary. A second degree burn usually becomes infected, but this may be averted by proper treatment.

again goes into a state of shock. It is profound and may follow neurogenic shock without an interlude. Beads of perspiration stand out on the patient's forehead, he is cold and clammy, his pulse is rapid, and his respirations are rapid and irregular. Blood pressure falls. This is secondary shock and is due to a loss of blood plasma. Blalock and others produced shock in experimental animals by traumatizing one of the hind-legs. After the death of the animal the traumatized leg was found to be heavier than the normal leg by about 3 per cent of the body weight. This increase in weight was due to a dilation, increased permeability, and rupture of capillaries, which permitted blood plasma and blood to pour into the traumatized tissue, causing hemorrhagic shock. When the leg of the experimental animal was burned instead of pounded, the same increase of weight occurred. In this case the exudate was not whole blood but blood plasma. The result was the same because the blood plasma is the most important part of the blood so far as osmotic pressure is concerned. This explains the high red blood count (6,000,000 or more), the high hemoglobin (16 to 17 Gm.), the low blood protein, and the extremely high hematocrit (almost all cells). The blood was thick and concentrated.

Underhill states that blood becomes thick and sticky, and the blood flow may be almost blocked. The blood has great difficulty in getting through the capillaries and is quickly robbed of its oxygen: the result is a partial asphyxia of the tissues. This in turn causes increased permeability of the capillaries. The hemoglobin content of seriously burned patients may go as high as 209 per cent. A sustained hemoglobin content of 140 per cent is almost invariably fatal. Fibrinogen emboli due to denatured fibrinogen caused by the heat may produce sudden death in burns.

The more extensive the burn, the more blood plasma is lost. This loss sometimes causes death in two to four hours. In addition, with plasma there is loss of sodium, chloride, and plasma proteins (mostly albumin) as well as calcium. There may be an increase in plasma potassium, magnesium, and bilirubin due to tissue and blood cell injury.

As a result of the burn, then, there results an increased permeability of the capillary endothelium, permitting the escape of plasma into the burned areas. The venous blood returning from this zone is concentrated. Although mostly albumin (rather than globulin) is lost, the blood still has a higher osmotic pressure than the intercellular fluid. Consequently this fluid is drawn into the blood stream only to be lost into the injured zone along with more plasma. Soon there is general hemoconcentration with stagnant anoxemia. The osmotic pressure in the blood is greatly reduced, fluid has been depleted from the interstitial spaces, and the blood is viscid. As anoxemia increases, tissue cells are damaged. Capillaries are leaky, and the brain takes oxygen because it is most vulnerable to anoxic states, thereby depriving the intestinal tract, liver, kidney, and muscle from their proper oxygen supply. This, in turn, produces the secondary effects of shock. Dextrose, which is broken down in muscle

TABLE III

TABLE OF SURFACE PROPORTIONS IN DETAIL
(From Lund and Browder: *Surg., Gynec. & Obst.*, 1944.)

AREA	AGE					
	BIRTH	1	5	10	15	ADULT
Head	19	17	13	11	9	7
Neck	2	2	2	2	2	2
Anterior trunk*	13	13	13	13	13	13
Posterior trunk†	13	13	13	13	3	13
Buttocks	5	5	5	5	5	5
Genitals	1	1	1	1	1	1
Upper arms	8	8	8	8	8	8
Forearms	6	6	6	6	6	6
Hands	5	5	5	5	5	5
Thighs	11	13	16	17	18	19
Legs	10	10	11	12	13	14
Feet	7	7	7	7	7	7
Total	100	100	100	100	100	100

*Without neck or genitals.
†Without neck or buttocks.

CLINICAL COURSE OF A BURN.—

The first stage is the *stage of shock*. The patient develops primary shock which lasts anywhere from two to four hours or longer. Coincidentally, or soon thereafter, secondary shock develops.

The second stage is the *stage of reaction and inflammation*. The patient usually reacts from shock. The burned area becomes fiery red and is extremely painful. There are fever and a rapid pulse. The patient is thirsty.

The third stage is the *stage of toxemia*. It may last for two or three days and may terminate in the death of the patient. The exact cause of the toxemia is unknown. It may be due to absorption from the burned area of toxic "H-substances" liberated by the skin necrosis which occurs, to the infection which inevitably follows, to dehydration, to "water intoxication," or possibly to a combination of causes.

The fourth stage is the *stage of septic toxemia*. Beneath the crusts (of plasma, serum, and cellular debris) which form over the devitalized skin, infection almost invariably occurs. This gives rise to pus formation with septicemia.

The fifth stage is the *stage of granulation*. Just as in any infected wound, healing takes place by second intention after local immunity has been established.

The sixth stage is the stage of *cicatrization*.

Stage of Shock.—We shall discuss the general subject of shock later (Chapter 14). The primary cause of neurogenic shock in a burned patient is pain. However, this type of shock is transitory and lasts only a short time. Then there is generalized vasoconstriction and a transient rise in blood pressure. Within an hour or more after a severe burn the patient

found toxemia from any cause, chemical (cincophen), bacterial (severe sepsis), or absorption of unidentified toxic products, may produce acute duodenal ulcers but not a true peptic ulcer. Dehydration may give rise to thick viscid bile, little mucus, and decreased pancreatic and intestinal juices, setting the stage for intestinal ulceration.

Most deaths from burns occur during the stage of so-called toxemia. There is much controversy concerning the existence of a toxin which circulates in the blood and which produces the devastating changes which are found. These changes may be due to a combination of dehydration, oligoplasmia, anoxemia, anuria, and infection. Some important events occur *in this stage and may be listed as follows:*

1. Destruction of red blood cells with a misleading fall in the hematocrit and possible hemoglobinemia and hemoglobinuria.

2. Focal central necrosis of the liver with a breakdown of liver function. This is said to be more regularly found when the burn has been treated with tannic acid. While it is true that the injection of 5 to 10 per cent tannic acid in rats will produce necrosis of the liver cells in the central portion of the lobule with hemorrhage and leucocytic infiltration, it is equally true that such changes do occur without the use of tannic acid, the latter probably the result of anoxemia and toxemia.

3. Cortical necrosis of the kidneys as well as destruction of convoluted tubules. This may result directly from anoxemia or toxemia or may be the result of hepatic insufficiency, renal insufficiency, or both. *Hepatic incompetency throws the entire work of detoxification on the* kidneys, injuring them. Anuria may result. (See Chapter 23.)

4. Adrenal focal necrosis and hemorrhage leading to adrenal cortical deficiency. Some observers have ascribed the low blood chloride, anhydremia, and low blood pressure to this lesion.

5. Pulmonary congestion and pulmonary edema. The cause of pulmonary congestion may be due to passive or active factors, the former principally through cardiac inadequacy, the result of decreased blood volume and hypostatic effects from immobilization. The latter is a compensatory mechanism which accompanies hyperpnea and an increased demand for oxygen.

Pulmonary edema may be the result of the following sequence of events: As a result of dehydration and hemoconcentration there is a stagnant anoxemia. Hyperpnea results from oxygen lack, increased accumulation of CO_2, and acidosis (q.v.) as well as the increased body temperature. Pulmonary capillaries become more permeable due to dilatation and anoxemia. These factors, together with an increased rate and amplitude of respiration, cause more fluid to leave the capillaries at first by *transudation* and later by *exudation*. Another explanation is based upon the rapid reabsorption of fluid and plasma from the burned area. The loss of fluid plasma from the burned area ceases after local tissues are distended to a pressure equal to capillary pressure. Usually this occurs within the first thirty-six to forty-eight hours. After five to

to carbon dioxide and water, goes only to lactic and pyruvic acid. The liver does not deaminize protein or produce glycogen in adequate amounts. The kidney does not excrete properly. Therefore there is an accumulation of fixed acids and amino acids and a depletion of glycogen with acidosis and azotemia.

The dehydration with loss of intercellular fluid soon leads to a depletion of intracellular fluid as well, with the appearance of increased amounts of potassium and phosphates in the plasma (see Chapters 11 and 12).

There is no vasodepressor substance in the lymph collected from the thoracic duct in burned animals. However, the exclusion of a toxigenic factor as a cause of burn shock has not yet been accomplished.

Stage of Reaction and Inflammation.—After twenty-four to forty-eight hours the patient usually has reacted from shock. A different picture now arises. Instead of a subnormal temperature, there is a rise to 102 to 105°. The tongue is dry, the skin is hot and dry, the blood pressure is up, and the urine is scanty.

The fever and thirst are due to a loss of water and plasma into the burned area and also to an insensible loss of fluid. In addition, no sweating occurs in the burned area or elsewhere in dehydration. (See Chapter 11.) Nitrogenous and other waste products cannot be efficiently eliminated unless there is water available for the formation of urine. When water is constantly lost through the dilated and permeable capillaries there is little available for urine formation. The results are dehydration, acidosis, and azotemia (retention of nonprotein nitrogen, uric acid, and creatinine). Thus the local inflammatory response increases hemoconcentration and dehydration, leading into the stage of toxemia.

Stage of Toxemia.—It is difficult to say how soon after the burn this stage begins. Probably within forty-eight hours and lasting ninety-six hours or more. The patient has absorbed some toxin that has its effect on the body as a whole.

Experimental work on the subject is difficult to interpret. In one experiment two dogs were used and their circulation crossed. One dog was burned; the other was unmolested. The burned animal died; the other recovered. Underhill and co-workers have shown that absorption does not take place from burned areas during the first thirty-six hours. Instead, fluid and plasma are attracted to the burned area. Our experiments show that some absorption begins within ten minutes through the capillaries and lymphatics. There is increased lymph flow during the first six hours. (See Chapter 11.) After thirty-six hours reabsorption takes place over a period of five to six days. In this regard burns react very much like other traumas or infections. The Underhill group felt that early symptoms resulted from dehydration, hemoconcentration, and loss of blood chlorides and serum protein and that the elevation of temperature is probably due to infection. Most experimenters have noted areas of necrosis in the liver. These may account for toxic symptoms.

Rarely the toxemia will cause a duodenal ulcer (Curling's ulcer).

The explanation for this is not entirely clear. Some believe it to be due to inactivation of Brunner's glands. Others believe it is due to toxic or infected bile. Pro

by facilitating reabsorption or by the introduction of fluids and plasma through the gastrointestinal tract or by parenteral means. It is evident that any treatment of extensive burns must take cognizance of the following important integrants: (1) Curtailment of the loss of plasma and electrolytes at the site of the burn no matter how extensive it may be; (2) restoration of lost plasma and electrolytes; (3) facilitation of dilution and excretion of toxins; (4) control of body temperature. If these primary disturbances can be modified, secondary effects such as hemoconcentration, anoxemia, hypochloremia, hepatic and renal insufficiency may be averted to a great extent.

Prevention of Plasma and Fluid Loss Into the Burned Area: This may be accomplished in many ways: (1) The entire burned area may be covered by sterile gauze over which sterile "mechanic's waste" has been placed. Elastic bandages are then wrapped over the area. The external pressure must not be tight enough to prevent venous return but sufficiently snug to increase intercellular tissue space pressure until it is equal to hydrostatic capillary pressure, thus preventing exudation. Indeed this leakage normally ceases if the stratum corneum is intact after the tissues are distended to a pressure equal to the capillary hydrostatic pressure. (2) The use of physiological saline solution into the burned area. This is thought to curtail the loss of plasma and electrolytes and also to make possible the dilution and excretion of hypothetical toxins, to control body temperature, and to prevent pulmonary edema and anuria. (3) A 5 per cent acqueous solution of tannic acid is still used by some with apparently good results. Tannic acid is sprayed on the burned area to form a tough crust. It is said to minimize the leakage of blood plasma and to delimit shock. Tannic acid has also been combined with silver nitrate. These solutions further the formation of a crust and relieve pain. In most cases, however, suppuration occurs under the crust. If it does, the crust must be removed and this is a painful and a traumatizing procedure. In addition, liver necrosis has been found more commonly in patients who have had tannic acid treatment, especially the continuous application as in the bath or jellies. Many other solutions have been advocated such as 1 per cent gentian violet. This is also a good antiseptic and forms a more pliable escar. (4) Saline bath. The patient is placed in a tub of warm water in which salt or boric acid has been dissolved.

The average bath tub holds 56 to 60 gallons of water and is ordinarily filled about two-thirds full. A quart jar of salt, or about two pounds, should be used. *Archimedes' principle:* When an object is wholly or partially immersed in a liquid it is buoyed up by a force equal to the weight of the displaced liquid and the center of pressure is where the center of gravity of the submerged portion would be if it were homogeneous.

Undergarments adherent to the burned area are removed. The patient is then left in the tub of isotonic saline solution two to four hours at a time, or continuously.

seven days if no infection ensues absorption is practically complete. It is possible, therefore, that after the third day there may be an excessive blood volume with a decreased urinary output resulting in pulmonary edema. Lastly, the lungs may fill with fluid if there has been too much intravenous therapy without regard to osmotic pressures.

6. The gastrointestinal tract has been mentioned previously as the site of ulcers (Curling's). These may be found in the duodenum and stomach.

Ordinarily dehydration alone may be surmised clinically by the brick-red skin which is loose due to loss of subcutaneous fluid. The mouth and tongue are dry and there is fever. Hemoconcentration gives rise to cyanosis due to stagnant anoxemia with an increased amount of reduced hemoglobin in the circulating blood. This state may lead to generalized edema, including the lungs because of the loss of plasma and the proteins. In burn toxemia any combination may be present making clinical signs unreliable.

Stage of Infection.—Theoretically infection should be prevented. It does not occur in first degree burns and can often be prevented in second degree but not in third degree burns. The skin assumes a dark color and sloughs away; the temperature takes a slightly elevated course. On about the fifth day after the burn crusts form over the devitalized and ulcerated areas. Beneath these crusts bacteria find an excellent medium for development. They multiply rapidly and produce an extensive infection. Then the temperature becomes septic in type.

Stage of Granulation.—If the crusts are removed, thick pus is encountered lying on granulation tissue, just as in any other wound that heals by second intention.

Stage of Cicatrization.—If the burn is of the third degree, the entire area will fill in with granulation tissue. The skin cannot cover the denuded portion because it is too extensive, consequently scar tissue helps fill in the area. Thus a vicious cicatrix may form.

TREATMENT OF BURNS.—There is no unified opinion concerning the management of extensive burns. Much has been written concerning the local treatment of the burned area as well as the general management of shock toxemia, infection, and the secondary results of these states. At the onset we may say that the various claims for local agents must be viewed in the light of the degree of the burn. If it is a first or second degree burn almost any agent will secure a healed uninfected wound. However, in third degree burns the size of the area is very apt to prevent healing by first intention and infection is difficult to avoid. It must be apparent then that the first consideration in the treatment of a burn is to prevent death from the greatest hazard; namely, shock.

Treatment of Burn Shock.—This treatment is based upon two important factors. First, every effort should be made to prevent the loss of plasma and electrolytes, and, second, such loss must be replaced either

available to prevent azotemia (best way to check this is to anchor a catheter and record hourly output), (d) pulse, (e) blood pressure, (f) respiration, (g) color of the skin, (h) dryness of mouth, (i) condition of lungs, especially edema. When in doubt the use of hypodermoclysis with physiological saline is safe.

Rhoads, Wolf, and Lee (quoted by Harkins) use Berkow's formula for estimating the per cent of body surface burned and give 50 c.c. for every per cent, giving one-third the first two hours, one-third the next four hours, and one-third the next six hours.

Harkins' rule: Give 100 c.c. of plasma for every point hematocrit exceeds 45. For children this should be reduced according to body weight. If plasma proteins are below 6 Gm., an additional 25 per cent should be added for each gram below 6.

Cope and Moore believe that fluid must be given to replace that which is lost through wound edema, from the wound surface, by the urine, and by insensible water loss. Their formula is used the first forty-eight hours which are the hours during which most fluid is lost. For wound edema they give a volume equal to 10 per cent of the body weight; for external loss, an amount varying according to the area of the wound surface: burns of 25 to 35 per cent, 1,000 c.c.; 35 to 60 per cent, 2,000 c.c.; 60 per cent and over, 3,000 c.c. Wound edema loss and external loss are added, and two-thirds of this combined volume is given as plasma and one-third as noncolloid isotonic electrolyte solution. The forty-eight hour period is divided into four parts: two parts are scheduled for the first twelve hours, one part for the second twelve hours, and the fourth part for the second twenty-four hour period. Calculations are made from time of burn. The reason for this is that the redistribution of fluid occurs most rapidly in the initial hours of the injury. For renal excretion, 1,500 c.c. of noncolloid fluid are allowed for each twenty-four hours, one-half to be given as isotonic electrolyte intravenously, the other half as glucose in water if given intravenously or as palatable fluids if given by mouth. For the insensible loss, 1,500 c.c. are given for each twenty-four hours or 3,000 c.c. for forty-eight hours of noncolloid electrolyte solution, glucose in water if given intravenously or palatable low salt fluids if given by mouth. A catheter is anchored and hourly outputs charted. Normal is 50 to 200 c.c. per hour. A falling or low hourly output (that is, 30 to 5 c.c. per hour) for three hours or more calls for immediate increase of fluid. Outputs of 200 c.c. per hour for more than six hours signify overtreatment if encountered in the first forty-eight hours or spontaneous diuresis if after the forty-eighth hour, and this amount calls for a cut in the amount of fluid given. The unreliability of this method, however, is evident when we come into the very low urinary output class because it is difficult sometimes to tell whether the therapy is inadequate or whether a renal lesion is present due to anoxemia, dehydration, hemoglobinuria, or damage antedating the burn which renders more output

In 1932 my colleagues and I experimented on guinea pigs. We burned them under sodium amytal anesthesia, then put some of them in various solutions: water, distilled water, normal saline, hypertonic salt solution, and tannic acid solution. The only guinea pigs that died were those that were not soaked. In this group, blood plasma was found on the pads placed in the little pans.

Badly burned patients do not perspire, either in the burned area or in the normal skin. This may be due to the collection of plasma in the intercellular spaces, drawing water out of gland cells, or to dehydration. Some believe it to be due to a sympathetic nervous system imbalance caused by the toxemia. Whatever be the cause, the heat-regulating mechanism is greatly impeded in its action (vaporization through sweating is the most effective means of controlling body temperature). A water bath has the additional advantage of helping to maintain an even body temperature and may prevent heat stroke from occurring during the toxemic stage.

Isotonic saline is about the best solution that can be used. It is not antiseptic and therefore some use 3 per cent boric acid solution. There is no difference in the results. Equipment to keep patients in tubs with thermostatic arrangement for an even temperature is desirable in the treatment of burns. The water should be 75° F. or about 24° C. Patients do not mind being in a tub of water; in fact, they like it. The patient should be left in the tub four or five days, until the stage of toxemia is over.

Patients in the toxemic stage frequently have an inordinately high fever. Since *there is dehydration, body water is not available for sweating, which would lower the* fever by evaporation. The control of the fever is a difficult problem. Some have suggested colon irrigations with cool water. This may result in shock or severe diarrhea. The bath treatment controls the fever fairly well.

There are apparatuses to lift the patient in and out of the water, so that the emunctories may act.

The Restoration of Fluids: If the patient can take fluids by mouth, this is the preferable way to administer them. In most instances of extensive burns this is not possible. Whole blood is needed to carry oxygen and to replace the cells which may be destroyed or lost. Parenteral restoration of fluids is especially indicated in addition to local arrest when the outer skin layers are destroyed, permitting generalized weeping. Plasma is most necessary because it is lost in greatest amounts. The quantity of plasma required may be enormous. Various "rules" have been used to determine the amount of plasma which should be given. No rule is infallible, and since it is the amount of circulating plasma which is important, a quick method of determining the circulating blood volume would be desirable. Even with this information it is the compensatory mechanisms which prevent or permit shock to occur (see Chapter 11). Therefore, at the outset we should say that it is the general condition of the patient which is the best guide. The factors to observe are (a) mental state (conscious or stuporous), (b) temperature—if normal, or nearly so, fluid is present for body temperature control by evaporation, (c) urinary output—if sufficient amounts of urine are excreted, enough water is

provide osmotic pressure but are also inert and therefore on theoretical grounds could not replace the labile active proteins. Their use is still in the experimental stage.

Noncolloid solutions such as physiological saline solution with or without glucose and distilled water with 5 per cent glucose are needed but must be given with sufficient plasma to provide for proper osmotic pressure relations.

If physiological saline solution is injected into the vein of a burned patient, it will leak out into the wound, because the capillaries are extremely permeable. This, in turn, will carry more blood plasma into the burned area, thereby increasing shock. Due to the great loss of blood volume, all arterioles constrict in order to keep up the blood pressure and by so doing force more fluid into the capillaries. Since the hydrostatic pressure in the capillaries is thereby increased and the osmotic pressure is diminished, the salt solution will leak not only into the injured area, but also into intercellular tissues all over the body. The result may be pulmonary and cerebral edema (water intoxication). The same thing may happen if too much water is given by mouth without salt. Blood transfusion is the treatment of choice. Recent evidence indicates that citrated blood plasma, alternated with whole blood, is good treatment to relieve the great hemoconcentration that exists. Blood plasma has a strong osmotic pull. This may not only prevent leakage, but also may attract body fluids into the thickened blood and permit a liberal intake of water by mouth.

The use of isotonic saline solution by hypodermoclysis is safe and for osmotic reasons will not be absorbed unless needed by the blood or unless instilled into tissue spaces under pressure higher than capillary blood pressure or 30 mm. of mercury.

Local Treatment.—The best treatment for small burns is the application of a sterile dressing with pressure as previously described. Blisters should not be opened. The bleb fluid has a protein content of 4.0 Gm. per 100 c.c. Albumin is in greater proportion to globulin than is present in the blood. Fibrinogen, prothrombin, and the diffusible portions of the electrolytes, carbohydrate, and nonprotein nitrogenous substances have the same concentration as that of the blood. Blister fluid rarely coagulates. This is thought to be due to the absence of thrombokinase. This lack of coagulation is important because water-soluble substances placed on the surface of a ruptured bleb will be absorbed. Conversely substances wihch permeate the capillary wall will be found in the bleb (Cope). The fluid in the bleb is usually free from virulent organisms. If the stratum corneum is intact even though killed by heat, it too forms a barrier against infection. Therefore, blisters should be allowed to remain intact and scrubbing of the wound should not be done, the latter because it is also traumatizing and adds to the shock. Later, after six days, as in the treatment of other wounds, q v., local attention to the wound may be given according to sound surgical principles.

impossible and moreover in which it would be dangerous to increase the fluid intake. To test this, a "water tolerance" test is used. One thousand cubic centimeters of fluid are given by vein in forty to sixty minutes, and if an increase in renal output occurs, the kidneys are not at fault and the therapy is inadequate. However, if no renal response occurs, then the kidneys are thought to be at fault and more fluid should not be administered.

Realizing that the hematocrit and protein determination may be normal yet the circulating volume greatly reduced (Chap. 11), we formerly used the following rule in conjunction with careful clinical observation q.v.: Since there are 23 c.c. of plasma for every pound of body weight, the total amount of plasma should be about 23 × body weight. Approximately 55 per cent of the blood is plasma and 45 per cent is cells. If the hematocrit goes up, then, to this degree, plasma may be said to be lost. Therefore, $\frac{\text{\% rise in hematocrit} \times (\text{body weight} \times 23)}{55}$ should roughly indicate the amount of plasma lost. For example, if the hematocrit is 55 and the burned patient's weight 100 pounds, then $\frac{10}{55} \times 2300 = 418$ c.c. of plasma needed as an initial amount. However, the frequent shifts of fluids make replacement by such rules impractical.

Other fluids: If the patient is able to take fluids by mouth they should be given provided an adequate amount of sodium chloride is allowed. It is the sodium which must be replaced (see Chapter 12), although some chloride is needed also. The excess chloride may be eliminated by the kidneys. Recently Fox has advocated the use of sodium lactate orally. There seems to be no proved advantage of this solution over sodium chloride. In all instances the oral administration of fluid should be correlated with careful estimation of plasma proteins and the clinical signs enumerated. A high protein concentrate like Amigen may be given by mouth to supply sufficient protein. However, in the emergency plasma proteins as such are also necessary and should be given as plasma by vein as needed.

Besides whole blood and plasma, other solutions may be used to provide fluid and osmotic pressure requirements. Albumin concentrate was used in conjunction with whole blood by some Army units. It, of course, does not provide globulin but is an excellent substitute for plasma. Solutions of amino acids are also employed by some. Since the liver is unable to deaminize the blood, there is already an excess of these products which depend upon the liver at least in part for their synthesis into usable proteins; therefore they have no place in the treatment of burns unless they may be given by mouth so that the selective absorption of the intestinal canal may assume its normal role. Nonbiologic colloids such as acacia, gelatin, and pectin have also been tried. Acacia is retained in the cells for years and may injure them. Gelatin and pectin

enough healthy skin to use. Grafts take due to the activity of the prickle cell layer of cells which move by pseudopodal prolongation. The stratum germinativum is perhaps even more important in this process. Nourishment is provided for the grafted tissue within about twenty-two to twenty-four hours by the capillary loops in the granulation tissue. The pressure dressings are not disturbed for eight days; then they are carefully removed. Then the area is exposed to the air for one to two hours and fresh dry dressings reapplied.

Burns of the hands constitute a special problem. The saline bath is perhaps best for such injuries. Early grafting of skin with pedicle grafts (as a rule) are necessary to prevent contractures. The hand is then placed in suitable splints.

Summary.—

1. Treat for shock
   a. Prevent loss of plasma
   b. Administer fluids, plasma, and blood as needed
2. Care for local areas after wound immunity has been established.
3. Use skin grafts as needed

Electrical Burns.—Electrical burns are deep and reactionless. Their danger is the electric shock, which may produce a paralysis of the respiratory or cardiac centers. The burn may not be noticeable for several days; then a large slough occurs. There is no special treatment.

Radium and X-Ray Burns.—These are extremely slow to heal. Sometimes they never heal, undergoing carcinomatous or sarcomatous change. All such ulcers should be widely excised. The denuded area may then be covered by mobilization of flaps or skin grafts.

Cold (Frostbite).—Frostbites are very much like burns in that they have a first and a second degree of severity. They are unlike them in one way that must be kept in mind. The blood vessels about the frostbitten area are constricted, causing the skin to turn white before destruction occurs. In addition to frostbite, there is, therefore, a lack of proper blood supply, with venous stasis and consequent thrombosis. The latter has been prevented experimentally by the use of heparin. This is more serious as far as local skin destruction is concerned than in burns, for in frostbites the area is anesthetized, permitting a longer action of cold. Davis studied the hands of aviators who had sustained high altitude frostbite. He describes a wet and dry type. The former occurs because blood enters the capillary bed where plasma is lost through dilated capillary loops. Dry gangrene results from acute peripheral vasoconstriction. Here the arterioles are full of blood and the capillaries are empty. The principal damage is to the endothelium of terminal capillary loops. Mild degrees of frostbite cause an increased permeability of capillaries. Severe injuries from cold are followed by thrombus formation at the arteriole-capillary junction. No thrombi are present in the

Over one hundred different substances have been used in the local treatment of wounds. These vary from simple oil to complex ointments, from isotonic saline bath to soaks in chemical mixtures and antiseptics. Recently sulfonamides which are absorbed (q.v.) and also penicillin jellies have been used. Lastly, such substances as casein, chemotherapeutic membranes and red blood cell pastes have been tried.

It is perhaps correct to assume that any nonirritating substance may be used and that it is rather the rest and infrequent dressings which contribute more to the wound healing than the particular substance employed.

In England the Bunyan envelopes are popular in the treatment of burns. They are made of oiled silk and are of different shapes. There is an inlet and outlet vent permitting thorough irrigation with different fluids. This is similar to our water bath treatment. Even after ulceration has occurred, the patient who has been in a tub of water may be left there if equipment permits; if not, he should thereafter be placed in the bath two or three times a day, for one or two hours, and allowed to rest between times in bed in a heat cradle, so that the sheets will not irritate the wounds. One-fourth per cent Chlorazene solution on the burned area prevents tough crusts from forming and decreases suppuration.

Adjuvants to Treatment.—Oxygen should be given routinely in extensive burns. This may be administered by tent, B.L.B. masks (if the face is not burned, or in an oxygen room. Morphine is necessary to control pain and should be used liberally. The sulfonamides may be given orally, rectally, or intravenously. They will find their way into the burned area readily. This is preferable perhaps to their local use where they may produce local irritation. However, ointments with sulfonamides have been extensively used. Penicillin is superior and should be given intramuscularly in 100,000 unit doses every four hours. The size of the wound in larger burns prevents healing by first intention. Infection creeps in. These drugs help until local immunity occurs. After local immmunity has been established (six to nine days), crusts may be removed. Blisters or blebs which have not ruptured spontaneously may be opened and loose, devitalized skin trimmed. If granulation tissue is healthy, free grafts (Thiersch, split-thickness, or Wolff) may be applied. Unhealthy granulations may be improved by the use of ultraviolet light. Edematous granulation tissue is best treated by pressure bandage with intermittent exposure to the air in a heat cradle (temperature 75° F.). It is absolutely necessary to use skin grafts in third degree burns to prevent viscious cicatrices from forming. If granulation tissue is old and fibrous, it should be excised and then grafted. A viscious scar must also be removed and the raw area covered by free or pedicled grafts (see Chapter 3). Autogenous grafts are used (homogenous, isogenous, and heterogenous grafts are not successful but the two former are sometimes used for the temporary covering they afford). It is often difficult to find

sures are intended to relieve vasoconstriction. They will succeed, of course, only where organic changes have not occurred but they may delimit damage to tissue.

A *chilblain* is a dilated and overdistended vein, with a small thrombus as a rule. Chilblains are painful and tend to recur upon exposure to cold. Warm wool covering for the feet prevents their formation and recurrence.

Immersion Foot.—Immersion foot is a term applied to a condition which results from long immersion of the feet (or, rarely, the hands) in cold water. In World War I the term "trench foot" was used for a similar condition. Men in life rafts or boats whose feet have been immersed in water for long periods are usually the victims. Contributory factors that influence its occurrence and severity according to Ungley are time of exposure, temperature of water (cold is worse, for there is thrombosis and gangrene), footwear (protects for a while but soon constricts due to swelling of feet interfering with circulation), immobility (moving about reduces liability to injury), body cooling, total immersion, repeated soakings or inadequate clothing reducing peripherocirculation, seasickness and starvation, age (men over 40 and under 17 are most susceptible).

There is a prehyperemic stage (one to four days). Extremities are cold, swollen, discolored, and numb with "glove or sock" anesthesia. Pulsations in the dorsalis pedis and posterior tibial arteries may be absent temporarily or permanently when gangrene occurs. The hyperemic stage which follows is characterized by swelling, especially if extremities have been warmed, sensory and motor disturbances, absence of sweating, blisters, ulcers, and gangrene. The posthyperemic stage (weeks to months) brings fresh blisters or infections and cold sensitivity. Treatment consists first of prophylaxis. Shoes and boots should be removed if wet, and grease applied to the feet. Care of the condition resembles that of frostbite, although the lesion occurs in warm waters. There should be no trauma (no massage or walking); warming of the feet must be gradual and slow

Chemical Injury

Acids.—Strong mineral acids (nitric and sulfuric), alkalies (lye), and weak organic acids (carbolic, Lysol, etc.) may cause ulcers on the skin or in the mouth or esophagus, through accident or suicidal intent. Such accidents are not uncommon in children. Of course, the bottles or cans are labeled "poison" but tots who cannot read get hold of them. They should be kept where children cannot reach them. An antidote for carbolic acid on the surface is alcohol. Iodine will produce a superficial burn. Even hydrogen peroxide continuously applied will cause necrosis. It is well to remember that if antidotes are not available, water is extremely useful. It washes irritants from the outside and dilutes them if taken by mouth.

capillaries in such cases. However, if vasoconstriction is released, blisters form and the stratum germinativum is lifted up. This is different from a first degree burn and indicates that cold penetrates deeper. Blisters, then, may mean a return of circulation at least temporarily. It may take six to ten months for the capillary bed to return to normal.

The intima of adjoining arteries is thickened as in endarteritis obliterans proximal to the arterioles. No thrombi are present here. Such *changes occur after* prolonged vasoconstriction.

A significant concomitant cause of the skin destruction is the fact that blood will not part with its oxygen when the skin is sufficiently cold (50° F. or 10° C.). (Lewis.)

Fig. 42.—Gangrene of both feet due to freezing. Boy aged 15 years. Healthy granulations are present. The gangrenous toes have been trimmed away. By this method of conservative care a maximum amount of surface tissue is saved. The granulations were grafted with split-thickness grafts.

Treatment of frostbite will depend on the degree of involvement and the severity of the injury. If extensive, a shocklike syndrome occurs, demanding treatment as discussed under burns. Heparin may be used to delimit the formation of propagating thrombi. Locally the method of choice is a gradual *increase in temperature*. The frostbitten part should be immersed in cold water first and then gradually the temperature may be raised. Warm water should not be used. It causes intense reaction, pain, and local sloughing. Also it is inadvisable to rub ice or snow on the part—*this traumatizes the already devitalized tissue.*

Control of atmospheric temperature is excellent if suitable equipment is available. A beginning environment of 20° C. which is slowly increased is desirable. Other methods are: applying heat to the body as a whole with generalized vasodilation, the action of drugs (amylnitrite, nitroglycerin, alcohol papaverine), drugs which act on the autonomic nervous system (nicotinic acid, mecholin), injection of sympathetic nerve trunks with procaine hydrochloride, and sympathectomy; all such mea-

The cause is an overactive sympathetic nervous system. Pulsations of the arteries remain. There is an increasing tendency to regard Raynaud's disease not as a clinical entity but rather as the peripheral manifestation of some more fundamental disorder, because achalasia of the

Fig. 43.—Raynaud's disease with scleroderma (symmetrical gangrene). Woman 38 years old. Middle finger of right hand has been amputated. Note the tapering fingers, which were moist, cold, and usually cyanotic. The skin is stretched tightly over the joints (sclerodactylia). Improvement followed intermittent arterial occlusion by cuff.

After a short period of time the disease progressed and cervical sympathetic ganglionectomy was done on both sides with great improvement. When last seen, no new areas of gangrene had resulted, although the patient reported that her skin was still stretched tightly over the fingers.

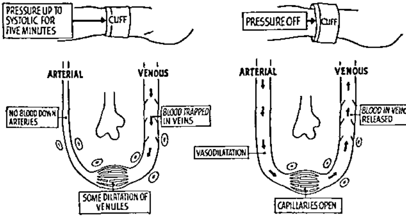

Fig. 44.—Diagram illustrating the effect of arterial occlusion in vasospasm. Pressure causes temporary paralysis of the vasoconstrictors, allowing vasodilatation when the cuff is released.

esophagus is not infrequently a complication; also idiopathic inflammatory reactions in skeletal muscle and the intestinal tract (regional enteritis may be part of this syndrome). The term acrosclerosis is applied to scleroderma and Raynaud's disease (see Chapter 20). Its symptoms have long been regarded as an example of how psychosomatic states

Injection of Drugs.—If more than 1 c.c. of Adrenalin is injected into a single small area, necrosis of tissue may result. This is due to interference with the circulation through arteriolar constriction. Ergot sometimes produces gangrene through its vascular effects. Neoarsphenamine will produce a slough if injected outside the vein.

Indirect Injuries Due to Circulatory Disorders

This group of pathological changes in peripheral vessels is known as peripheral vascular disease and forms an important part of hospital clinical work and private practice.

Venous Congestion

Varicose Veins.—Varicose veins are discussed under the heading of "Veins" in Chapter 17.

Arterial Causes

Functional.—

This may be *vasodilatory* as in Weir Mitchell's erythromlalgia but does not produce necrosis or gangrene. It is often associated with organic diseases of the blood vessels.

In *Raynaud's disease,* usually seen in women, a continual constriction of the vessels produces gangrene of the fingers or toes. This is also known as symmetrical gangrene because it affects both extremities simultaneously. The fingers turn white when cold and red when warm; then they became blue, due to stasis in the venules. They are cold and painful. A related though milder condition is *acrocyanosis* usually seen in young neurotic women. In its most severe form, erythrocyanosis frigida, small round ulcers may appear on the lower legs. Usually, however, the hands and feet are cold and moist with varying degree of cyanosis. Eczematous lesions may be present. Acrodynia (painful extremities) is seen chiefly in infants 9 to 18 months of age. The fingers and toes become swollen and erythematous with a pinkish color. Vasomotor phenomena are present and the child is emotionally disturbed.

Livedo reticularis also causes cyanosis in the extremities, chiefly the lower. It has been called livedo racemosa, livedo annularis, and asphyxia reticularis. The etiology, like Raynaud's disease, is probably primarily an organic or functional spasm of the arterioles with dilation of the capillaries and venules. This gives rise to patchy constant areas of cyanosis on the legs and feet. There is coldness, numbness, and dull aching sensations in the feet.

Rarely a disease known as scleroderma is seen associated with Raynaud's disease. The skin is stretched tightly over the finger joints (sclerodactylia) and appears smooth and glossy. Such patients are said to be "hidebound." Scleroderma may be associated with cardiospasm and stenosis at the cardiac end of the stomach due to fibrosis (achalasia). Fibrosis of the lung may occur also. Is regional ileitis related too? Ergot may produce gangrene due to prolonged constriction of the vessels.

beginning as purely functional disorders may result in severe organic disease. The vascular changes in Raynaud's syndrome are not necessarily due to active vasoconstriction but may result from vasodilatation in the palmar arch with a diversion of blood from the fingers and passive collapse of these vessels. The underlying disease may be organic, vascular, severe secondary anemia, or syphilis.

Treatment must first include a careful search for underlying causes as previously mentioned and the care of such disorders. In addition, measures should be instituted for the relief of vasospasm. These include the application of constriction in the upper arm and leg. It is well to use a sphygmomanometer cuff, inflating it up to systolic pressure (about 130 mm. of mercury) and leaving it on for fifteen to twenty minutes at a time. This is said to produce temporary vasoparesis due to inhibition of vasoconstrictors with vasodilation. In severe cases cervical or lumbar sympathetic ganglionectomy must be done. (See Chapter 18.) Results, however, have not been uniformly good. There is temporary improvement following operations of sympathetic denervation. Hands become warm, pink, and dry. All discomfort leaves, but there often is a recurrence. This may happen in a month to a year. It may be due to the action of adrenalin on the denervated vessels but is more probably the result of reinervation from a peripheral nerve or associated ganglia.

Cervical sympathectomy may be performed as follows: An incision is made from the seventh cervical vertebra downward along the border of the scapula. The trapezius muscle is split, the rhomboids are retracted, and the lumbodorsal fascia is cut transversely. The third rib for

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cause residual vasospasm is less apt to occur. He therefore divides the sympathetic trunk below the fourth ganglion, encases the decentralized second and third ganglia in a silk cylinder, and sutures the distal end into the muscle (curved arrow in diagram shows division and displacement below the third ganglion). An incision is made medial to the border of the scapula extending from the second to the fifth thoracic spinous processes. The lumbodorsal fascia is divided. The trapezius is divided longitudinally and the rhomboid obliquely, and the longissimus dorsi (longissimus cervicis division) is divided as shown or split longitudinally, as is also the iliocostalis cervicis muscle. A section of the third rib is removed and the transverse process is rongeured away. The pleura is then separated from the vertebral column to the midline and also from the rib for a short distance beyond the line of resection. The second rib is then treated in a similar manner and the intercostal muscles are divided transversely with care so that the intercostal vessels and nerve are not injured. If the chain is severed below the fourth ganglion, then the fourth rib is resected instead of the second. The third intercostal nerve is picked up and divided laterally and then followed medially to the intervertebral foramen, dividing the communicating rami from the anterior, then posterior branch of the intercostal nerve. The posterior branch is divided and then the anterior branch is followed to the arachnoid and divided. Spinal fluid may leak out but is controlled by placing a small piece of Gelfoam over the leak. The first, second, and fourth nerves may be dealt with similarly and the sympathetic ganglia removed or treated according to the Smithwick technique.

B. The entire lower extremity may be denervated of its sympathetic control by removing the first, second, third, and fourth lumbar ganglion. If the first lumbar ganglia are removed bilaterally, loss of ejaculation is apt to occur. This is less likely if the second ganglia are removed The first lumbar ganglion lies inferior to the renal vessels under a layer of fascia in the costovertebral angle. The third ganglion usually lies just above the common iliac artery. We usually employ a retroperitoneal approach because it can be done bilaterally. The slightly oblique incision is made above the level of the umbilicus The external oblique is divided to the edge of the rectus. In obese individuals the rectus muscle may also be divided. The internal oblique and transversalis muscles are divided in the direction of their fibers and the peritoneum is gently reflected from the quadratus and psoas muscles. The genitofemoral nerve is an important landmark, for it lies lateral to the sympathetic chain. The rami are divided and the sympathetic chain removed In obese people in whom it is necessary to remove the first lumbar ganglion, a posterolateral incision very much like that used for nephrectomy is useful.

(Modified from deTakats, G., Surg., Gynec., & Obst. 79: 359, 1944.)

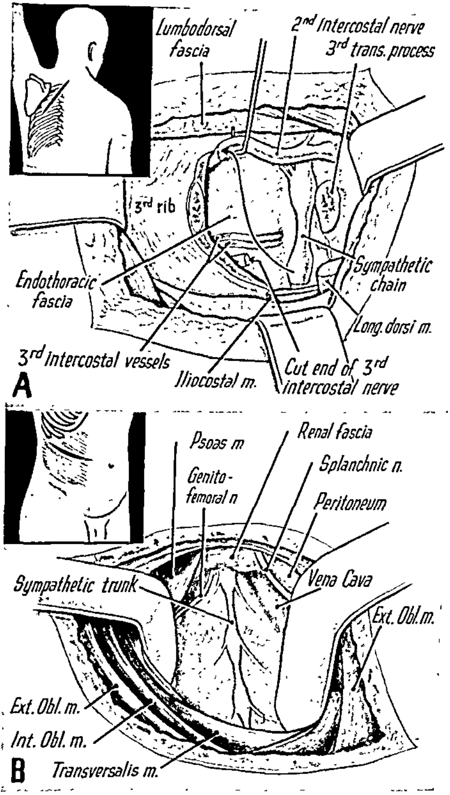

Fig. 45.—A. Sympathectomy of the upper extremity may be accomplished by removing the inferior cervical and first, second, and third thoracic ganglia. Since many synapses are present in these ganglia, the procedure is largely postganglionic in type. Residual vasospasm due to sensitization of smooth muscle to adrenalinlike substances does occur in some cases. Smithwick recommends that the synapses be preserved be-

(Continued on opposite page)

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(Modified from deTakats, G.: Surg., Gynec., & Obst. 79: 359, 1944.)

a distance of about three inches is resected along with the transverse process. The pleura and endothoracic fascia are peeled forward and the second and third intercostal nerves are pulled out and the anterior and posterior roots are sectioned intradurally proximal to the dorsal ganglia. A small segment of nerve is taken out. The dural defect may be sealed with a small piece of Gelfoam. All rami are cut. The sympathetic chain is cut below the third dorsal ganglion and this ganglion is removed. The chain is then tied, turned under, and sewed to muscle. For a gangrenous finger or toe, amputation is necessary.

Sudeck's syndrome is a vasomotor dysfunction of peripheral vessels usually following some minor trauma to the wrists or ankle. Various names have been used to identify the condition: chronic traumatic edema, trophic edema, traumatic angiospasm, post-traumatic osteoporosis, reflex causalgia-like states, peripheral trophoneurosis, reflex nervous dystrophy, acute atrophy of the bone. (See Chapter 21.)

The underlying cause is not clearly understood but the condition is thought to be due to the following sequence: pain due to trauma with resulting hyperemia, improper attention to the injury with voluntary splinting to avoid pain, stasis due to immobility, reflex vasoconstriction (due to pain or axonal reflex), increased pain due to swelling and tissue anoxia, more splinting, more stasis, etc. Undoubtedly there is some injury or at least chronic stimulus to the sympathetic as well as to sensory nerve fibers.

We have seen in Chapter 3 that the usual effect of injury is vasodilation. Since the same nerve fibers which are subservient to protopathic sensibility may cause opposite effects on stimulation, it may be assumed that the degree of chronicity of pain, together with local nerve involvement, makes up some of the complex components of the problem. In other words, there is a chronic stimulation of somatic and efferent vasoconstrictor fibers or dilator fibers if present.

The symptoms and signs include pain, which is localized but spreads as the syndrome progresses, hypersensitiveness, decrease in arterial pulsation, swelling, vasodilation and redness or cyanosis and coldness (vasoconstriction), the latter is less common, motor weakness, stiffness, and later bone atrophy.

Trophic changes are of two types: (1) The skin is cold, thin, and glistening, the superficial layers are denuded, and sweating is profuse. There is loss of hair, tapering of the digits like in Raynaud's syndrome, and clubbing of the nail; vasoconstriction is present; and the skin temperature is two to six degrees lower than in the normal extremity. (2) The more frequent type presents a warmer extremity, with more hair, edema, glossy skin, and no clubbing, although the skin may be dry and even scaly.

Treatment includes prophylaxis which means rest and immobilization for a suitable period for minor injuries and infections. The disease

usually responds to sympathetic block with 1 per cent procaine. However, the effect is not lasting as a rule, and if there is no response, then sympathectomy will not help. Recently tetraethyl ammonium bromide and Priscol have been used. If the syndrome is well advanced, sympathetic ganglionectomy is the procedure of choice. Those who believe that chronic vasodilatation is the cause attribute the relief from sympathectomy to an interruption of pain fibers. In those cases which are accompanied by vasoconstriction the patients are thought to receive the benefit from an increased blood flow. Indeed, warm moisture helps those with vasoconstriction and cold moisture is of benefit to patients with chronic vasodilation. Those with trophic changes are benefited, depending upon

Fig. 46.—Gangrene (dry), due to ergot poisoning. The patient, a woman aged 18 years, had a miscarriage and was given ergotamine tartrate by intramuscular injection.

restoration of blood flow to normal and therefore are helped by cold or warmth, depending on whether there is vasoconstriction (warmth) or vasodilation (cold). Not all cases can be explained on changes in blood flow and are either nerve phenomena or psychalgias. (See Chapter 28.)

Organic Causes of Gangrene.—

Arteriosclerosis.—Arteriosclerosis includes a group of chronic changes in the arteries which are identified pathologically as follows: (1) Atherosclerosis, which begins in the *intima* with splitting of the elastic fibers, some destruction of fibrous connective tissue and even muscle, and deposit of lipoids followed by fibrosis, hyalinization, atheroma, and

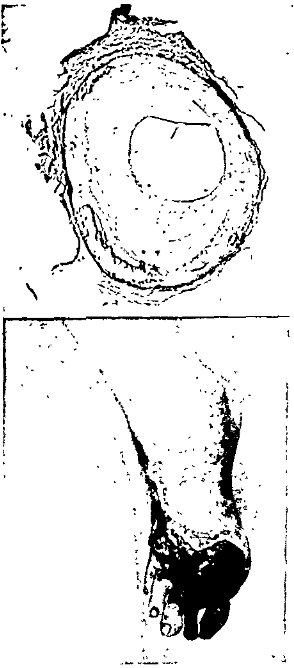

Fig. 47.—Arteriosclerotic (dry) gangrene (Mönckeberg's type). A cross section of a partially obliterated artery is shown. There are calcification of the media and thickening of the intima, with almost complete occlusion by the thrombus.

calcification. The deposition of lipids in the intima is dependent on local factors not clearly understood but thought to be related to defective fat metabolism. Atherosclerosis is a disease caused by the presence of an irritant which is thought to be an excess of cholesterol, in ester form, which is brought to the arterial intima in phagocytic cells rather than by inhibition. The absence of atherosclerosis in youth is said to be due to an effective removal of excess esters from the intima in the atheroma of infancy and puberty and at the sites of congenital abnormalities and injuries. Local thrombosis may occur at the site of the atheromatous plaques, giving rise to occlusion at the site of thrombosis or distally due to dislodgment, producing an occlusive embolism. The bifurcation of the aorta is a common site for the formation of ragged plaques leading to thrombosis and slow occlusion of the lumen. Thrombosis may also occur in the presence of dissecting aneurysm, arteritis and congenital narrowing. (2) Medial sclerosis (Mönckeberg), which is also called senile arteriosclerosis. It affects chiefly the smaller arteries such as the femoral, radial, temporal, popliteal, etc. The first change is a fatty degeneration of the muscle and elastic coat with necrosis and calcification. This is manifested as "corduroy" arteries if the calcific rings are separated or "pipe stem" if fused. These changes may be felt and also seen in the x-ray film as areas of calcification. (3) Endarteritis obliterans or deformans, which is an occlusion of the artery by connective tissue without atheroma or calcification. It is the same process as atherosclerosis but occurs in smaller vessels. The artery may become converted into the fibrous cord. (4) Diffuse arteriolar sclerosis (arteriocapillary), which is characterized by endothelial hyperplasia, hyalinization, and reduplication of elastic lamellae (Karsner). It is found in the arterioles of the kidney, liver, brain, gastrointestinal tract, skeletal muscle, adrenal gland, pancreas, and other organs but is not a cause of gangrene of the extremities. Clinically the term arteriosclerosis obliterans has been used to identify the type which leads to progressive occlusion of arterial lumina. It supplants the terms thromboarteriosclerosis obliterans, occlusive arteriosclerosis, arteriosclerosis with thrombosis, senile gangrene, diabetic gangrene, and endarteritis obliterans.

Symptoms and Signs.—Usually arteriosclerotic gangrene is seen as the Mönckeberg type which causes a gradual decrease in the blood supply of the extremity, producing dry gangrene or mummification. This is a slow shriveling process in which the part changes from a cyanotic color to black. The part is painful during this process. Finally a line of demarcation occurs between the living and dead tissues. Ordinarily there is some inflammatory response with hyperemia proximal to this line. Of course, there is no pulsation in the dorsalis pedis or posterior tibial or even in the popliteal artery as a rule. The atheromatous type may give rise to similar symptoms or if the thrombus becomes dislodged, there may be a sudden and dramatic change as is seen in embolic gan-

grene which may be "wet" or "dry." One of the earliest symptoms is an intermittent claudication. When exercised, the muscles of the leg demand more blood, and when this is not forthcoming, a painful spasm results. Slow occlusion of the aorta at its bifurcation gives rise to the following symptoms: pain in both legs and hips, effortless fatigability, and intermittent claudication.

Nocturnal cramps may simulate intermittent claudication, but the phenomenon is not limited to the aged or those who have peripheral vascular disease. It is observed in aged patients with arteriosclerosis that when the blood pressure falls due to rest and when in addition there is venous stasis due to lack of motion, a relative histanoxia occurs producing painful muscle spasm. This is seen in the second trimester of pregnancy and in young men and women apparently normal. This pain is like that of angina pectoris (Lewis). If at a certain level of work (metabolic demand) the oxygen available is insufficient, pain arises. Since the cramps occur while the person is at rest, the events are as previously stated or there may be other factors such as hypoglycemia

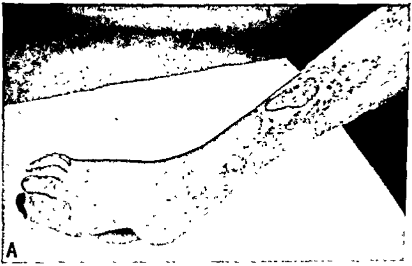

Fig. 48.—Early arteriosclerotic gangrene and varicose ulcer. Man aged 67 years. No pulsation of the dorsalis pedis or posterior tibial artery could be felt.

and hypocalcemia; either or both may induce muscle cramps, the former because oxygen is useless to working muscle cells unless there is enough dextrose to be oxidized and insulin to catalyse the reaction. Therefore diabetic patients on a diet providing too low a dextrose level have muscle cramps. The latter is seen in tetany to a marked degree. Often heat is used to relieve the cramps, especially in the aged with arteriosclerosis. This usually makes matters worse because tissue metabolism is increased, demanding more blood which is not forthcoming. Most of these patients have found that cold does not help either because blood holds its oxygen in cold, and if any normal collaterals are present they are forced into spasm. The patient therefore will get out of bed and walk for a few minutes, stimulating venous return and thereby breaking a vicious circle (see Chapter 17). Muscle cramps disappear promptly, permitting a resumption of sleep.

X-ray shows the calcification of the vessels which usually may be identified especially in the radial artery.

Tests for Peripheral Circulation.—*Arteriography* is useful in arteriosclerotic occlusion, embolism, thromboangiitis, vessel trauma to demonstrate the site of occlusion,

and the amount of collateral circulation; also, it demonstrates arteriovenous aneurysms and simple arterial aneurysms (the position of the sac and its degree of patency). It may also detect the presence of bone tumors (Shallow) and is useful as an aid in diagnosing venous occlusions. Usually 7 to 10 c.c. of Neo iopax, thorotrast, or Diodrast are injected into the brachial or femoral artery and then an x-ray film is made. This test, while very useful, is *not without danger*. Complications both local and general have been reported. In the *former* group may be mentioned hematomas, extravasations, and severe vasomotor reactions as well as local thrombosis with subsequent gangrene. The latter occur whether Thorotrast or organic iodine compounds are used. Hematemesis, severe anemia, decreased coagulability of the blood, and sudden death from respiratory failure have been reported. Necrosis of organs especially rich in reticulo-endothelial cells (liver and spleen) from Thorotrast is known, and its radioactivity may be maintained in these cells for years. There may also be erythematous eruptions, nausea, vomiting, cyanosis, and respiratory distress.

Oscillometry consists of applying a sphygmomanometer cuff and observing the differences in pulsation of the extremities, the amplitude, and the level at which no oscillations are seen. The instrument known as an oscillometer (Pachon) is especially made for the purpose. Obviously the extent of collateral circulation is not revealed by this test. *Venous return test.* The arm or leg is elevated to empty the veins. Then with the extremity in the horizontal position a blood pressure cuff is applied and inflated to about 60 mm. of mercury. Normally the veins fill in five to ten seconds. A delay implies partial arterial occlusion.

Changes in Skin Temperature.—If the body temperature is normal and if the room temperature and humidity are known, then the skin temperature may be accurately measured and compared with the opposite extremity. Mercury skin thermometers and an electrical device known as the Dermatherm are available for this purpose. It is useful when there is a sudden drop in one extremity or when great variations exist between the two extremities or between adjacent areas. A temperature rise after tests to relieve spasm may help estimate the amount of the spastic element.

Determination of the spastic element may be elicited by drugs, spinal or general anesthesia, local infiltration of the nerves to the part, sympathetic nerve block, sacral block, or artificial fever induced by foreign protein or typhoid vaccine; also, immersion of the hands in hot water (110° F. for thirty-five minutes) will normally cause the feet to reach a temperature of 90 to 92° F. Another test which is very simple is the application of the blood pressure cuff to the principal artery, inflating it to systolic blood pressure and leaving it in position for five minutes. When released a normal extremity will flush evenly in a few seconds. This will be delayed and uneven in diseased vessels. The intradermal injection of histamine, 0.1 c.c. of a 1:1000 solution, will not produce a flare if an insufficient pressure is present in the skin vessels or if spasm is severe. Another method for determining the spastic element is the use of drugs. Formerly tetraethyl ammonium chloride and tetraethyl ammonium bromide were employed to act as sympatholytic drugs. They did produce vasodilation but they had the disadvantage of having to be used subcutaneously or intramuscularly. Recently a newer product has been developed whose trade name is Priscol (Ciba). The drug is priscoline hydrochloride. It is a 2-benzylimidazoline hydrochloride. Its action is to produce vasodilation and to increase peripheral blood flow, and it is said to counteract the constrictive effect of epinephrine-like substances in the vascular myoneural junctions. The drug, of course, has a general effect, and it is apt to produce a general vasodilation with fall in blood pressure. Priscol may be given in 25 mg. doses and may be used orally or parenterally at three- to four-hour intervals. If there have been no distressing side effects, the drug may be increased to 50 mg.

For tests to determine the spastic element, 200 mg. are given in divided doses of 50 to 100 mg. every hour. After administration, the following tests help to evaluate the presence of the spastic element: (1) The skin temperature; a gross estima-

tion of the differences between extremities as well as between the distal portion of the extremity and the skin of the body may be done either with the back of the hand or with an electrothermometer. The difference in temperature between the toes and the abdominal wall or the fingers and the skin over the sternum should be greatly decreased *after the use of this drug*, and this change should occur within about five minutes after intravenous administration and twenty minutes after intramuscular injection and within forty-five minutes if given orally. (2) Dependent venous filling; if the patient is kept recumbent with his legs elevated at an angle of 45 degrees for a few minutes, normally the veins collapse. Blanching of the skin is greater, of course, in peripheral vascular disease where there is less blood in the extremity at all times. If the patient sits up, allowing his feet to hang over the edge of the bed, the skin flushes and the veins distend with blood. Ordinarily the veins will fill within about 10 to 20 seconds. If it takes a longer time, say 40 or 50 seconds, for the veins to fill completely, there is presumptive evidence of impaired arterial circulation. By the use of sympatholytic vasodilators and adrenolytic substances such as the drug mentioned, flushing time will be decreased as will also venous filling time. It is conceivable that in advanced arteriosclerosis Priscol may be harmful because blood may be shunted into vessels that do have a spastic element and thereby divert blood elsewhere than from the extremities. (3) *Oscillometric readings should be increased after vasodilators if the spastic element is present.*

Priscol comes in tablets of 25 mg. each or in vials of 10 c.c. with each cubic centimeter containing 25 mg. The other drugs previously mentioned which have been used to interrupt vasospasm by blocking the sympathetics are tetraethyl ammonium bromide or tetraethyl ammonium chloride. These drugs are given intramuscularly in the dose of 20 mg. per kilogram of body weight. A 10 per cent solution 100 mg. per cubic centimeter is used, and the maximal dose ranges from 1 to 1.2 Gm. Clinical symptoms and signs are, after all, most reliable. The maximal blood flow to the foot may be reduced to 50 per cent without symptoms or trophic changes; 67 per cent is apt to produce them.

Whereas in dry gangrene nature may ultimately perform its own amputation without death of the patient, in moist gangrene this usually does not occur. Dry gangrene may become moist after invasion by saprophytic organisms. Both types harbor pathogenic bacteria, the former usually fewer than the latter. The terms dry and moist are clinically descriptive and do not always indicate the cause or degree of infection. Indeed there may be no initial infection in some types of "wet" gangrene as in gangrene due to embolism. It is more common where infection plays an important role as in diabetic gangrene with infection or gangrene due to virulent bacterial invasion without primary vascular changes. The moistness of the part is due to the presence of lymph, blood plasma, serum, and exudate, depending upon its cause. In embolic gangrene a sudden occlusion with its concomitant spasm traps blood due to a decrease in vis a tergo, venospasm, or venous thrombus (here the "wetness" would be chiefly plasma). In infections which are primary the cause is exudation. The extremity turns deep purple and blebs form, and before the leg turns black it is very malodorous. The "wet" type is more dangerous because of the greater virulence of the infection.

Prevention and Treatment.—Present concepts do not point to a clear way of preventing arteriosclerotic gangrene. First a word of caution concerning surgery of any kind on the lower extremities of elderly

people. This should not be done without careful evaluation of the circulation. A gangrenous process often begins after minor operations such as bunionectomy, removal of ingrown toenail, trimming of corns or calluses, etc. Obviously the same warning applies to any peripheral vascular disease. However, in the pregangrenous stage much may be done to *alleviate pain, promote collateral circulation, and at least postpone the* development of gangrene. Since the extremities comprise about 56 per cent of the body surface and contain no vital organs, they are important in the regulation of body heat, rate of blood flow, and blood pressure. Improvement in their circulation is important not only to the extremity involved, but also to the body as a whole. The general condition of the patient demands careful attention.

In arteriosclerotic gangrene the element of spasm is minimal. Therefore, chemical vasodilators help very little. However, they may be tried. Alcohol may be given in repeated small doses by mouth, acetylcholine or papaverine hypodermically. The lumbar sympathetic ganglia may be injected with 1 per cent procaine (20 c.c.). If a favorable response (vasodilation) is obtained, lumbar sympathetic ganglionectomy may be done. Even though this does not prevent further involvement of vessels by the arteriosclerotic process, it does postpone the approach of gangrene and it does relieve pain, because pain results from a demyelinization of somatic nerve fibers caused by anoxemia due to poor vascularization. For the same reason motor nerves do not function properly and reflexes are impaired. Hot and cold contrast baths and elevation and lowering of the legs (vascular exercises) are helpful. Mechanical devices such as the glass boot have been advocated. This is a positive-negative pressure apparatus which is thought to "pull" out new collaterals and force a return of blood and lymph by the veins and lymphatics. The rationale is comparable to that of "Bier's hyperemia" methods. It is best used at room temperature. Many fear its use because of the possibility of (1) dislodging venous thrombi which may be present, (2) spreading infection if cellulitis is a complication, (3) actually causing arterial occlusion at the site of the cuff, if arteriosclerosis or endarteritis exists—a possibility which contraindicates the use of tourniquets during amputations in such states, or (4) actually traumatizing the poorly nourished skin, thereby favoring infection.

Another mechanical method which is very useful is that of intermittent venous occlusion. This is effective not only because of the increase in capillary pressure, but also because of the reactive hyperemia due to accumulation of metabolites, as described by Lewis and Grant.

Many devices are available which cause inflation (less than diastolic pressure, about 40 mm. Hg) for one to two minutes and then deflation for about one and one-half to two minutes. They are allowed to work continuously; that is, day and night. This increase in venous pressure is *transmitted back to the arterioles* or their collaterals, causing them to

open up or stimulating the formation of new capillary loops. If such pressure were too high or too long continued, the capillaries would rupture, causing deep hemorrhage and necrosis.

If the pressure were kept as high as the diastolic blood pressure continuously, a condition similar to Volkmann's contracture would follow. The cuff is therefore inflated (up to diastolic pressure or below) and then decompressed: that is, pressure is applied intermittently. Pressure up to systolic may cause a thrombus to form at the site of the cuff.

Ligation of femoral vein is indicated in chronic obstructive arterial disease before gangrene, ulceration, or infection occur. Glasser reports relief of pain in the majority of cases so treated. This procedure does not prevent gangrene but may delay it and afford relief. It is also effective in reducing the likelihood of pulmonary embolism following amputation. For slow occlusion, resection of the constricted area has been advocated by Leriche if sympathectomy does not relieve symptoms.

Treatment for Gangrene: Arteriosclerotic patients usually present themselves for treatment when gangrene of one or more toes has occurred. These should be amputated with local anesthesia and then treatment as previously outlined should be pursued. The wounds should be left open. Usually but not invariably this is a beginning which leads to more and more involvement of the foot and legs.

Two tests which serve as a guide for the site of amputation are (1) the determination of cutaneous temperatures and (2) production of histamine flare. The latter is by far the more reliable. Should no response to histamine occur, circulation is inadequate and $\frac{1}{10}$ c.c. of hydrochloride histamine or histamine acid phosphate in a 1:1000 solution should be given. The response occurs within five minutes and manifests itself by hyperemia and rise in skin temperature. This test is by no means infallible. In colored patients the rise in temperature must be the guid*ing sign. A word of caution concerning these tests should be made.* If they are positive, the stump may still fail to heal and if they are negative, good healing may yet be obtained if atraumatic surgery is used. When gangrene involves the foot and lower leg, amputation just above the condyles of the femur should be done. This is the site of election regardless of whether or not the popliteal artery is pulsating. However, the *best test is an incision in the lateral muscles of the leg without a tourniquet; if bleeding is ample, the stump will heal.*

We have frequently performed amputation below the knee in the hope of saving the knee joint and the upper third of the tibia; also through the foot so that the ankle joint may be saved. Subsequent amputations were necessary in many cases. With modern artificial legs, in this age group it is much better and safer to amputate high enough for healing to occur. A circular incision is made, without a tourniquet, the vessels are ligated, muscles are severed at a slightly higher level, and the femur is sawed about two to three inches above the skin incision. Muscles and

skin are loosely approximated. In a few cases lower leg amputations will be successful provided there is active bleeding when incision is made in the muscles. When in doubt, we begin our test incisions immediately above the gangrenous area and perform amputation at the first site of active bleeding. The patient is up and out of bed on the following morning.

Types of anesthesia: We have usually used a light ether anesthetic. Recently refrigeration anesthesia has been employed with success.

Cryo- or crymotherapy has been discussed in previous chapters. Its use in badly infected, gangrenous extremities has been a great help. The leg is wrapped with gauze around which are placed ice bags or ice water or ice. Cellular activity is suspended by this method. Absorption of toxins is reduced, bacteria do not grow, and pain is greatly relieved. Oxygen consumption of tissues can be reduced about 13 per cent for each degree centigrade. If, in addition, a tourniquet is applied, the oxygen demands are reduced sufficiently so that necrosis is prevented for many hours. Blalock has recently demonstrated experimentally that if a tourniquet is necessary, cooling an extremity prevents or at least lessens the chances for shock by curtailing the rapid loss of plasma into the injured extremity. In previous chapters some of the objections to cold were reviewed and especially when employed in inflammatory lesions. In gangrenous extremities the local effects which may inhibit inflammation and local immunity factors are not important. The greatest consideration is the improvement in the patient's toxic state, the reduced fever, and the chance to restore water balance and prepare the patient for surgery (especially in diabetic gangrene). After forty-eight to seventy-two hours operation may be safely attempted. Using this method Allen has performed amputations relying entirely on refrigeration for anesthesia. A narrow tourniquet is applied, and the entire extremity is packed in ice, and within two hours amputation may be done. A slight modification of this is the use of two tourniquets, two to three hours before surgery. One is placed immediately above the area of gangrene and the second above the site of the proposed amputation. It is applied to the stump postoperatively for several days.

We have used this method but prefer packing the leg up to the knee in ice for two to three days and then amputating quickly without a tourniquet under light ether anesthesia.

Our objection to the tourniquet-ice method is the necrosis of the stump distal to the tourniquet, making the process of healing very slow and potentially dangerous in debilitated patients.

Diabetic Gangrene.—Diabetic gangrene is a form of arteriosclerotic gangrene with or without infection. Since infection is more common in diabetic patients, this is apt to be a complication if not the cause of necrosis.

The arteries show a subintimal thickening and lipoid degeneration. This may extend well into the intima. However, there may be calcific changes in the media and necrotic fatty plaques. In any event, the vessel lumen is narrowed, and finally there is occlusion by secondary thrombosis.

Acute venous occlusion and phlebosclerosis are not as common in persons with diabetes as in those without diabetes. Diabetes is not always associated with arteriosclerosis, especially if the disease has been prop-

open up or stimulating the formation of new capillary loops. If such pressure were too high or too long continued, the capillaries would rupture, causing deep hemorrhage and necrosis.

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without a tourniquet and under light ether or sodium pentothal anesthesia. This should be of the "chop" or guillotine variety or if infection has not spread rapidly, the short flaps may be very loosely closed with one-half inch gap.

EMBOLIC GANGRENE.—Embolic gangrene may be associated with arteriosclerosis in which atheromatous plaques or thrombi become dislodged. Usually the vascular tree is normal. The causes are:

Heart Lesions.—(1) Mural thrombus in the left atrium due to (a) rheumatic heart disease with mitral stenosis and (b) degenerative heart disease with auricular fibrillation, (2) infarction of left ventricle from coronary occlusion, (3) thrombosis upon the heart valves in acute endocarditis, and (4) subacute bacterial endocarditis, (5) failing heart from any cause. In over 90 per cent of the cases of myocardial infarction, the ventricles (especially the left) are the site of thrombus formation. In rheumatic heart disease the thrombi are in the auricles and auricular appendixes. Cardiac mural thrombi are more common in older patients with auricular fibrillation and/or congestive heart failure.

Paradoxic or Cross Embolism: This refers to those which are originally in the venous system and come to lodge in the arterial side. This may occur in patent foramen ovale or patent interventricular septum where alteration of pressure may be higher in the right than in the left atrium or ventricle. Venous thrombi occur postoperatively or in various infections such as typhoid fever, pneumonia, diphtheria, malaria, puerperal sepsis, and influenza. They may follow fractures, operations, and infections in the chest.

Arterial Lesions: (1) Atheromatous plaques with thrombi, (2) trauma to an artery resulting in thrombosis with subsequent embolism, (3) aneurysm, and (4) inflammation. Thrombosis causing embolism may be due to inflammatory disease (thromboangiitis obliterans, periarteritis nodosa, mycotic arteritis); degenerative changes (arteriosclerosis); traumatic injury (cervical rib, gunshot or other penetrating wounds, contusions); and thrombosis without arterial disease (infectious diseases, heart disease, blood dyscrasias, ligation or suture of artery, idiopathic thrombophilia as seen postoperatively without apparent cause, and trauma).

Subacute bacterial endocarditis and auricular fibrillation are the most common causes. Often a "saddle" embolus lodges at the bifurcation of a vessel. If this occurs at the bifurcation of the aorta, both legs may have symptoms and the area of discoloration and coldness extends to the level of the umbilicus. Finally, a part of the embolus becomes dislodged, affecting one leg only and sparing the other. Recently we have had a case where the embolus divided, lodging in the common iliac bifurcations on both sides. The prognosis is better in all arterial occlusions if a large vessel is occluded, for it permits collaterals to form. It is serious in end vessels, such as the mesenteries, where gangrene is usually inevitable.

Immediately after an embolus lodges the affected vessel and the regional arterial tree go into violent spasm. The embolus may be smaller than the lumen of the artery but is trapped by its spasm. Within two

erly controlled in comparable age groups. However, there is a definite tendency for arterial change with calcification to occur earlier in persons with diabetes.

Symptoms and Signs.—There is usually a history of some trauma to the foot or some minor surgery inflicted by the patient in trimming corns or toenails. A small sore then results which is painless but fails to heal. The area becomes larger, finally involving one or more toes which gradually undergo shrinking as in "dry" gangrene with a definite line of demarcation. More often the same story is told as to the onset, but the process is more rapid with redness, swelling (wet gangrene), and lymphangitis. Soon large blebs which are purplish in color form on the plantar surface. Small joints become infected, as do the phalanges and metatarsals. This is followed by general cellulitis and septicemia. There is no pulsation in the dorsalis pedis and posterior tibial and often none in the popliteal.

Prevention and Treatment.—Diabetic patients must be instructed in the care of their feet. The slightest scratch should be regarded seriously and cared for by rest in bed, elevation of the extremity, and intermittent venous occlusion.

If infection is not present, a gangrenous toe may be amputated after a line of demarcation has formed. If infection is the cause of necrosis and collateral circulation is good, attention should be given the infection which may heal. The sulfonamides and penicillin are invaluable here. Moist hot packs are undesirable because of the trauma incurred by their application and the maceration of tissue which may result from prolonged soaks. Heat is not advisable for the same reasons plus those discussed previously (q.v.).

If infection and vascular occlusion are present, conservative measures should be tried. However, they will usually be unavailing because diabetes is difficult to control in the presence of infection and infection is not apt to subside in the presence of uncontrolled diabetes. As a practical course it is advisable even under such conditions to prove to the patient that local and conservative measures will not produce a cure. In rapidly spreading infection in the presence of vascular occlusion diabetic coma is apt to follow. This is extremely difficult to handle. Attention to water balance, blood and plasma transfusion, electrolyte control, and insulin are necessary adjuncts. In addition, penicillin should be given in large doses intramuscularly, 100,000 units every three hours. Conservative amputations should be tried but may fail because the stump will not heal. Certainly in gangrene of the toes or foot amputations like the Lisfranc (disarticulation of the tarsal and metatarsal joint), Chopart (disarticulation of the mediotarsal joint), or Syme (disarticulation of the ankle joint) should be given a chance. Above the ankle it is far safer and better to pack the extremity in ice for twenty-four to forty-eight hours then do an amputation just above the condyles

vasoconstriction, stasis, and anoxemia of the part, thereby causing irreversible changes to capillaries and cells. Usually the part is protected by "mechanic's waste" as a pad, surrounded by bandage, and exposed to room temperature. If amputation is anticipated, cold should be used as described under arteriosclerotic gangrene.

If the patient is seen early, say within six to twelve hours, embolectomy should be done. We have successfully removed emboli of the aorta after twenty-three hours. Some surgeons state that this procedure may be

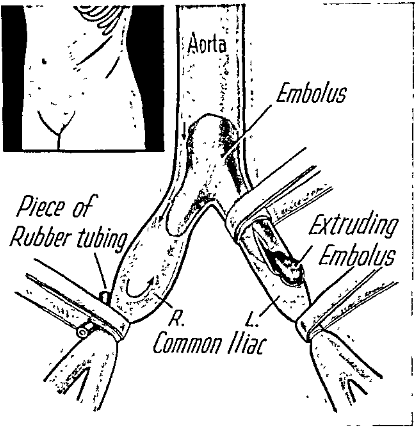

Fig. 49.—Embolectomy. Diagram of procedure used in a recent case of saddle embolus at the bifurcation of the aorta. M. G., a woman age 62 years, had auricular fibrillation. The large embolus caused bilateral occlusion of the iliacs. Within six hours following the onset of symptoms the right leg began to show signs of returning circulation. The left leg was cold, mottled, and slightly cyanotic. The color change and temperature change extended up to the umbilicus on the left side. The diagnosis was obviously a saddle embolus at the bifurcation of the aorta and the patient was operated upon at once.

Note the incision is a modified McBurney incision on the left side. The peritoneum was pulled medially. The aorta and both common iliacs were exposed. Umbilical tape was placed around the left common iliac above and below the proposed site of incision and around the right common iliac. All tapes were tightened. A longitudinal incision was made in the left common iliac artery and the left lower tape was released. Bleeding was free. Then the upper left tape was released, but no bleeding occurred for a few minutes. Soon the force of the blood stream, together with the dilation caused by the increased pressure below, forced the saddle embolus into the left common iliac where it found free egress from the longitudinal incision. It was prevented from descending down the artery by the distal tape. After a free flow of blood occurred from the proximal side, the upper tape was pulled taut and the artery was flushed with heparin solution. The incision was then closed with interrupted mattress eversion suture of 0000 silk. This patient made an uneventful recovery. Circulation was restored to both legs. Pulsations ultimately occurred in both legs, although the left dorsalis pedis did not show pulsations for approximately three weeks. (Case of Dr. R. M. Vandivier.)

hours a propagating thrombus distal to the embolus begins to form. This may be so extensive after a few hours that many collaterals are occluded so that even the removal of the embolus would not permit adequate circulation for the extremity. It is because of this phenomenon, together with the effect of spasm on the arterial wall, that sympathetic nerve block has been advocated.

Symptoms and Signs.—The symptoms and signs are first those of the underlying condition. Pain is usually present. It is sudden and severe, especially if the patient is ambulatory. It extends along the entire leg distal to the embolus and is probably due to vasospasm and muscle ischemia. Therefore it is more prominent in active muscles than in those which have been at rest in bed. Peripheral pulses are absent, the leg or arm is pale with scattered areas of cyanosis, and it is cold, with parasthesia, diminished reflexes, and some paralysis. The embolus is usually located in the first bifurcation of the principal arteries above the upper limit of physical findings. The area in between is normal due to ample collateral circulation. After a time even these vessels may become thrombosed, causing an increase in the area involved by gangrene; the gangrene is usually dry, especially if blood flow is not entirely arrested at once. Often it is wet with the formation of large bullae.

Treatment.—A sudden occlusion of an artery, with vasospasm of collateral vessels, will so decrease the vis a tergo of the blood that stagnation will occur in the veins, which stand out and soon become thrombosed. Usually the vessels are healthy except for those affected. Spasm, therefore, plays an important role. There is an emergency so far as the extremity involved is concerned. If it can be nourished until collaterals form, the leg may be saved. It is here that the glass boot or pavex machine, if used early before thrombi form or infection occurs, may help. Intermittent occlusion is much better. The surgeon should be slow to amputate because he must (1) improve the general condition of the patient, which is apt to be serious; (2) allow venous thrombi to become fixed, so that they will not be dislodged and carried into the blood stream (this and the possibility of spreading infection make use of pavex dangerous); (3) permit collateral circulation to form; (4) allow infection to localize; (5) allow nature to repair damaged tissue as far down as possible with the aid of new collaterals.

The extremity should be elevated so that edema of the muscles will be lessened. It is argued by some that elevation makes the blood flow through narrowed arteries against gravity. Since muscle demands far more blood than skin or subcutaneous tissue, it becomes edematous when circulation is slow or stasis occurs in veins. Edema, then, results, preventing the entrance of blood except under considerable pressure. Heat should not be used below the site of occlusion. This increases the metabolism of the part, calling for more blood which is not forthcoming. Heat above the site may improve collaterals. Cold should not be used. True it does decrease the demand for blood, but it may increase

gical treatment because the uninvolved vessels carry the blood supply; namely, radial and ulnar, dorsalis pedis, and posterior tibial.

After eight to ten hours the embolus becomes attached to the intima and antispasmodics may be used or the vasoconstrictors inhibited to accomplish vasodilation and stimulate collateral circulation. The following measures have been employed:

(1) Papaverine hydrochloride, ½ to 1 grain (0.03 to 0.06 Gm.), intravenously repeated at hourly intervals if necessary during the first twelve hours; continuing dose is ⅓ grain intramuscularly every six hours, (2) paravertebral block of the sympathetics with 1 per cent procaine, or sympathetic ganglionectomy, (3) actual excision of the portion of the artery containing the clot (Leriche) if twenty-four hours have elapsed since the occlusion or if the endothelium under the embolus is severely damaged or if gangrene threatens despite embolectomy.

Embolectomy is done under local, spinal, or general anesthesia. It should be done at the earliest possible moment through a liberal exposure. Wide umbilical tape is placed around the artery distal to the embolus to prevent its dislodgment distally. The artery is mobilized, and the adventitia is infiltrated with procaine and stripped off for a liberal distance. A proximal temporary holding tape is now placed around the artery. A longitudinal incision is made between encircling ligatures or special clamps or both, and the clot is gently "milked" out or allowed to come down by temporary removal of a proximal clamp or sucked out by catheter. Great care is exercised not to injure the intima. The clamps are then removed and the tapes loosened, and if a free flow of blood occurs from the proximal and distal portions of the artery, it may be assumed that the lumen is patent. The tapes are again tightened. Through the incision which has been made in the vessel between the occlusive tapes, the interior of the artery is flushed with 100 mg. of heparin dissolved in 10 c.c. of physiological saline solution; then another 100 mg. of heparin is dissolved in 10 c.c. of physiological saline and is introduced above the proximal occlusive ligature. This is acomplished by loosening the tape temporarily and occluding the artery with the fingers. The solution is injected and then the occlusive ligature is quickly tightened. This is done with the hope that thrombosis will not occur at the arterial suture line or the site of the anastomosis. The artery is then closed with interrupted sutures of 00000 silk, approximating intima to intima as described in Chapter 3. Following the operation, heparin may be given by the intermittent intravenous method or by the continuous intravenous method. If the former is used, the recommended dose is 50 to 100 mg. of heparin every four to six hours intravenously until coagulation time has been prolonged to about fifteen minutes. Another method of administration is the continuous intravenous method whereby the solution is given in 5 per cent glucose or physiological saline to which 100 to 200 mg. of heparin have been added per liter. About 20 to 25 drops are

of doubtful value, especially in small arteries like popliteal, because there will be a tendency for local thrombosis as a result of intimal irritation by the embolus and by its removal. It is true that collaterals may form quickly and abundantly. The immediate relief of arterial spasm is stressed by most authors. One may question the rationale for this since vasoconstriction is a protective mechanism in the presence of an embolus (a) to prevent entrance of small embolic fragments into smaller vessels less capable of forming collaterals and (b) to hasten the formation of collaterals by increasing proximal hydrostatic pressures. Preoperative sympathetic nerve block and spinal anesthesia and even papaverine may cause relaxation of the artery distal to the embolus, permitting a fragment to slip down into much smaller branches in which surgery is less effective, and if surgery is not done, collaterals are less apt to form. It should be noted, however, that the embolus becomes fixed in a few hours Antispasmodics and sympathetic block may be used before this time as a *diagnostic* procedure provided that embolectomy is to be done immediately.

Fig. 50.—Embolic gangrene (wet gangrene with infection).

This is permissible because vasospasm proximal to the embolus makes localization of the embolus difficult. There are other difficulties in localizing an embolus because collateral circulation may make the embolus appear more distal. The propagating thrombus peripheral to the embolus also confuses in the same way. The heart is frequently irregular and feeble in its beat, making the pulse difficult to detect.

Emboli usually lodge at bifurcations or divisions of arteries because their lumina become smaller at such points. Skin temperature changes provide a helpful but very unreliable guide. Usually if the popliteal is involved, the line of coldness is found above the ankle; an embolus at the bifurcation of the femoral shows this line at the junction of the middle and lower thirds of the thigh; and if in the common iliac, the line is at the junction of the middle and upper thirds of the thigh; if at the aortic bifurcation, the cold area extends to the level of the umbilicus. The arm behaves in a similar way. Emboli in paired arteries rarely require sur-

and other internal vessels, even in the retinal blood vessels, but this is rare even in late cases. The upper extremities are not involved as often as the lower. Arteries and veins after thrombosis may recanalize, giving rise to periods of remission and exacerbation. Smaller and larger vessels may be simultaneously involved. After the organization of the thrombus the walls of arteries and veins become thickened and infiltrated involving the accompanying nerve. The femoral and anterior tibial arteries are most commonly involved. Unlike arteriosclerotic gangrene, the process begins very insiduously with the formation of a small ulcer and with general thickening of surrounding tissue rather than shrivelling of the part.

Ulcers are apt to come and go. Often the patient states that the ulcer started by trimming a toenail too short or cutting a corn. Two of our patients had small burns of the dorsum of the foot and one sustained frostbite. A good rule to remember is that all patients should have a

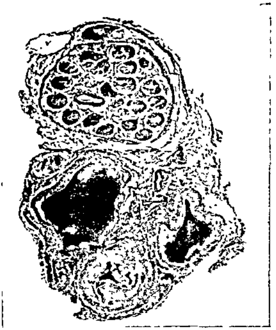

Fig. 51.—Buerger's disease. Cross section, showing the fibrosis around the arteries, veins, and nerve. Note the thrombi in the thickened vessels, obliterating their lumina.

careful examination of the extremities before minor surgery of the feet is attempted. In the younger group thromboangiitis or diabetes may be present; in the older, arteriosclerosis with impending gangrene. Patients with diabetes as well as others in these groups must be carefully instructed as to the care of their feet—the slightest injury or operation may start the formation of the ulcer with subsequent spread of the area of necrosis.

A thrombosis of an artery or vein involving the nerve presents a trying problem because of excruciating pain. Since a larger vessel is usually involved, there is good chance of a collateral circulation forming, if the patient can tolerate the pain. These men are young, usually heavy smokers, with hyperactive sympathetic nervous systems. *Intermittent*

given per minute, the total dosage being about 200 to 240 mg. per twenty-four hours. A third method is the intermittent intramuscular method whereby the drug is given intramuscularly about 100 mg. every eight hours or about 1 mg. of heparin per pound of body weight initially and subsequently 0.5 to 0.7 mg. per pound of body weight. We have used heparin as Depo-heparin sodium made by Upjohn in the following way: An initial dose of 200 mg. of heparin is given immediately after surgery. Usually this plus the heparin which has been injected intra-arterially is sufficient for an initial dose. The coagulation time is tested four hours after surgery and if necessary the aqueous heparin sodium is given intramuscularly in the dose of 100 mg. Usually, however, this will not be necessary because the Depo-heparin maintains a prolonged coagulation time for approximately forty-eight hours. In the past we combined this method with Dicoumarin which was given orally, using an initial dose of 300 mg. and then repeated as needed at four- to eight-hour intervals. However, Dicoumarin is perhaps more toxic and must be checked by prothrombin time, whereas heparin may be checked by simple coagulation time method. Therefore, we have been using the combined preparation of aqueous heparin and the Depo-heparin and depending upon this for our effect. The Depo-heparin is then given every other day for a period of about seven days, sometimes longer, depending upon the recurrence of emboli or the indications. See Chapter 13.

The approach to the bifurcation of the aorta is made through a left lateral oblique incision as for lumbar ganglionectomy. The peritoneum is retracted to the right.

Thromboangiitis Obliterans (Buerger's Disease or Presenile Gangrene).—This usually occurs in the lower extremities of middle-aged and younger persons. In this disease both the arteries and veins are blocked by thrombi. The nerve is also involved, producing excruciating pain. Pulsation is absent in the dorsalis pedis and the posterior tibial artery.

Etiology.—The cause of this disease is not known. Indeed it may be a combination of vascular diseases. There is, however, one significant probable cause and this is smoking. The effect of smoking on peripheral vascular disease is probably due to vasoconstriction caused by nicotine or the repeated short periods of anoxemia incident to the inhalation of smoke. This is shown by pallor, reduced temperature, and lowered volume of the extremities after smoking. The disease has been observed in a 15-year-old boy who was a heavy smoker.

There is first an arteritis, an inflammation of unknown etiology, with almost immediate thrombus formation. Sometimes a phlebitis migrans (migratory type) precedes or accompanies the disease. The extremities go through color changes, due to temperature changes. When allowed to hang down, the extremity is very painful and red (erythromelalgia). Buerger's disease is differentiated from arteriosclerotic gangrene by the younger age of the patient, the intractable pain, the low blood pressure, and the x-ray picture (absence of calcification). The disease may occur in the abdominal

salt solution intravenously, and sodium tetrathionate, 1 Gm., with sodium thiosulfate, 0.6 Gm., in 10 c.c. distilled water, to increase the oxygen content of the blood (chemical and mechanical), and rest. Pain may be controlled by injecting the sensory nerves to the part with alcohol. *Morphine* is not given because of the danger of addiction. If the patient can "weather the storm" of pain, he may avoid gangrene and amputation or at least postpone it. Sympathectomy is of value in many cases. The sympathetic ganglia should be injected with 20 c.c. of a 1 per cent procaine solution. Usually the first lumbar is all that is necessary, but if there is no response, the second and third may be injected also. A favorable response includes return of pink color, warmth, and absence of sweating. Each toe should be examined carefully. If a toe remains cold

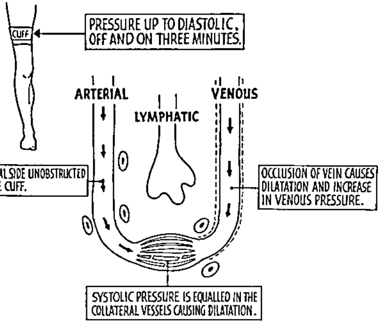

Fig. 53.—Diagram illustrating the effect of intermittent venous occlusion in the treatment of organic disease of the arteries. The pressure must not exceed diastolic, for it would not only interfere with the inflow of blood, but might damage the diseased vessel as well. The optimum pressure is about 40 mm. Hg on for 1½ to 2 minutes and off for about the same time This varies in different cases. The treatment may be continued night and day, without disturbing the patient

and blue and moist, sympathectomy will hasten gangrene just as heat does, but it will permit an amputation of the digit with a good blood supply to the stump. If the response is good, sympathetic ganglionectomy is done—first, second, and third dorsal for the arms and second, third, and fourth lumbar for the legs. Thrombophlebitis is a common complication of sympathetic ganglionectomy (4 per cent) in the heparin-resistant phase.

The treatment after gangrene has occurred is amputation. In this disease as much tissue as possible should be saved because all of the vessels are not diseased. Amputation of a gangrenous toe may be followed

claudication (a limp that develops upon exercise, due to the demand for more blood to the muscle than the crippled circulation can supply) is an early and annoying symptom. Intra-abdominal thromboangiitis obliterans causes intermittent intestinal claudication which manifests itself as severe cramping pain after eating. "White, red, and blue toes," due to the effects of temperature or dependent position, are also a warning sign.

Treatment.—The treatment at this early stage is the elimination of smoking (chemical?), the use of intermittent venous occlusion, vascular exercises, and antispasmodics (spasm), excessive amounts of 5 per cent

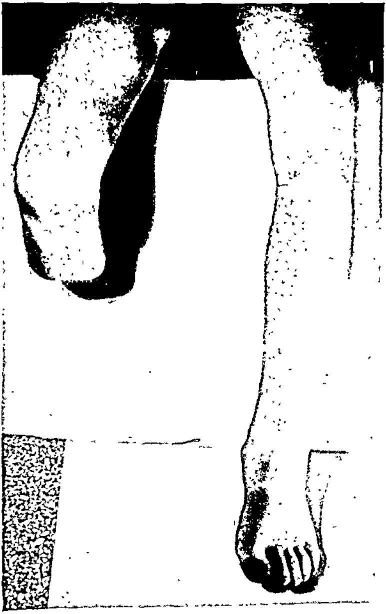

Fig. 52.—Buerger's disease. The patient is a young man aged 28 years. The *right* leg had been amputated previously. Note the deep color of the foot (erythromelalgia) when hanging in a dependent position. There is gangrene of the big toe and second toe. No pulsation in the *dorsalis pedis or posterior* tibial arterie. The popliteal can be felt faintly. There is excruciating pain. Amputation was ultimately done.

salt solution intravenously, and sodium tetrathionate, 1 Gm., with sodium thiosulfate, 0.6 Gm., in 10 c.c. distilled water, to increase the oxygen content of the blood (chemical and mechanical), and rest. Pain may be controlled by injecting the sensory nerves to the part with alcohol. *Morphine* is not given because of the danger of addiction. If the patient can "weather the storm" of pain, he may avoid gangrene and amputation or at least postpone it. Sympathectomy is of value in many cases. The sympathetic ganglia should be injected with 20 c.c. of a 1 per cent procaine solution. Usually the first lumbar is all that is necessary, but if there is no response, the second and third may be injected also. A favorable response includes return of pink color, warmth, and absence of sweating. Each toe should be examined carefully. If a toe remains cold

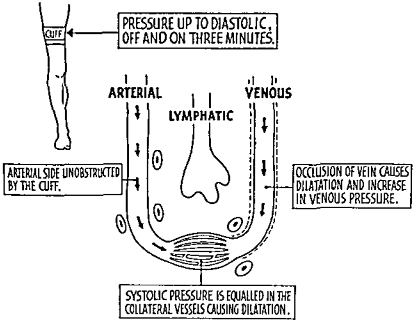

Fig. 53.—Diagram illustrating the effect of intermittent venous occlusion in the treatment of organic disease of the arteries. The pressure must not exceed diastolic, for it would not only interfere with the inflow of blood, but might damage the diseased vessel as well. The optimum pressure is about 40 mm. Hg on for 1½ to 2 minutes and off for about the same time. This varies in different cases. The treatment may be continued night and day, without disturbing the patient

and blue and moist, sympathectomy will hasten gangrene just as heat does, but it will permit an amputation of the digit with a good blood supply to the stump. If the response is good, sympathetic ganglionectomy is done—first, second, and third dorsal for the arms and second, third, and fourth lumbar for the legs. Thrombophlebitis is a common complication of sympathetic ganglionectomy (4 per cent) in the heparin-resistant phase.

The treatment after gangrene has occurred is amputation. In this disease as much tissue as possible should be saved because all of the vessels are not diseased. Amputation of a gangrenous toe may be followed

claudication (a limp that develops upon exercise, due to the demand for more blood to the muscle than the crippled circulation can supply) is an early and annoying symptom. Intra-abdominal thromboangiitis obliterans causes intermittent intestinal claudication which manifests itself as severe cramping pain after eating. "White, red, and blue toes," due to the effects of temperature or dependent position, are also a warning sign.

Treatment.—The treatment at this early stage is the elimination of smoking (chemical?), the use of intermittent venous occlusion, vascular exercises, and antispasmodics (spasm), excessive amounts of 5 per cent

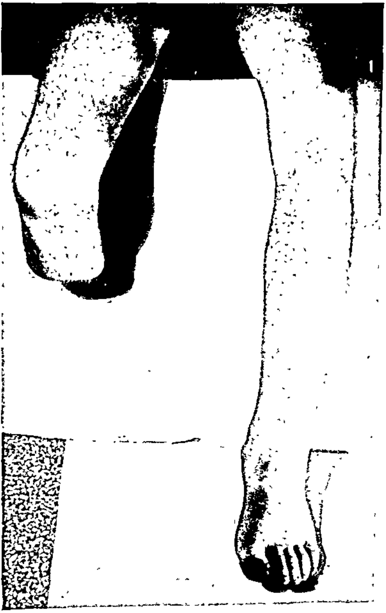

Fig. 52.—Buerger's disease. The patient is a young man aged 28 years. The right leg had been amputated previously. Note the deep color of the foot (erythromelalgia) when hanging in a dependent position. There is gangrene of the big toe and second toe. No pulsation in the dorsalis pedis or posterior tibial arterie. The popliteal can be felt faintly. There is excruciating pain. Amputation was ultimately done.

Local Causes.—

1. Increased hydrostatic pressure—thrombophlebitis or phlebothrombosis, varicose veins (involving the deep as well as the superficial veins), arteriovenous fistula, cicatricial occlusion as is sometimes seen following radical mastectomy; orthostatic edema occurs in old and debilitated patients or after prolonged immobilization of the extremity in a cast as in fractures.

2. Obstruction to the lymphatic return occurs in perilymphatic fibrosis from malignant disease, in filariasis due to the mechanical irritation of the Filaria worm in the lymph channels, cicatricial occlusions from ulcers, burns, or other injuries and from congenital anomalies of lymph vessels, lymphedema praecox or congenital lymphedema (hereditary or familial—Mulroy's disease, and simple types which affect only one member of a family).

3. Increased capillary permeability is due chiefly to infection.

Edema in infections (see Chapter 5) is due to an increased augmented permeability and the resultant increase in plasma protein in the tissue spaces. Reabsorption is prevented by the higher than normal osmotic pressure of the tissue spaces and also by thrombosis of blood and lymph capillaries. Heat causes increased vasodilatation and therefore the exudation of more plasma into the involved area, thereby aiding localization. From our previous discussion it is apparent that pressure bandage is contraindicated because it prevents adequate plasma bathing of tissue spaces and forces absorption of toxic material before local or systemic immunity is established. Active motion is also contraindicated because it too forces proteins into the lymphatics and aids in this propulsion. In addition there is the danger of dislodging thrombi. Elevation of the infected extremity is indicated because it limits venous stasis and edema and permits lymphatic absorption in an orderly manner. Therefore, rest and elevation of the part are favorable aids in the management of excessive inflammatory edema. Normally if 5 c.c. of normal salt solution is injected intradermally it should disappear in forty five minutes. In edema it will disappear more rapidly (due to high osmotic index of the fluid); in anasarca, almost immediately (McClure Aldrich test). The disappearance time sharply decreases just before or coincident with edema and increases preceding the edema or with its subsidence.

4. Combinations. In phlegmasia alba dolens there is probably venous and lymphatic obstruction. Acrocyanosis and Raynaud's disease may cause edema due to a decreased vis a tergo and therefore venous stasis or local tissue anoxia or capillary dilatation with increase in capillary permeability. In cellulitis there may be associated lymphedema. Unilateral edema of the extremities is usually due to (1) venous obstruction, (2) lymphatic stasis (congenital or acquired), (3) mixed venous and lymphatic obstruction, (4) arteriovenous fistula (congenital or acquired).

Swellings *not due to edema* in *one* extremity are seen in (1) pseudohypertrophic muscular dystrophy, (2) neurofibromatosis, and (3) tuberous sclerosis (see Chapter 16). Swellings not due to edema in *both* extremities are due to lipedema or abnormal distribution of fat in the lower legs for which condition dieting and exercise is indicated.

by complete healing. If gangrene or sepsis is present, a higher amputation is necessary. This may be below the knee at the site of election or through the condyles. Gritti-Stokes amputation is the best type because it gives a good weight-bearing surface in a young person who will need it.

Edema of the Extremities

Edema prevents the normal interchange of nutrient material and waste products between the blood tissue cells and therefore predisposes to infection and ulcers.

Edema of the lower extremities may be due to the following causes: (1) decreased osmotic pressure of the blood, (2) increased hydrostatic pressure in the capillaries, (3) increased permeability of the capillary wall, (4) obstruction to the lymphatic return (see Chap. 11), (5) combinations of the foregoing, and (6) miscellaneous.

The causes may be further divided into general and local. The more common varieties are as follows:

General Causes.—

1. Decreased osmotic pressure—nephrosis, malnutrition, hemorrhage, chronic infected areas, or any condition producing hypoproteinemia; an increased amount of saline or other crystalloids diluting plasma proteins; salt block. (Chapter 11.)

2. Increased hydrostatic pressure—cardiac decompensation, ascites with incompetent deep and superficial veins in the legs.

3. Injury to capillary walls—nephritis, organic arterial disease where there are asphyxia and capillary dilatation, excessive heat which causes great peripheral dilatation, allergic states such as angioneurotic edema, vitamin deficiencies such as scurvy, toxemias due to chemicals such as arsenic, etc.

4. Combinations of foregoing as in arteriosclerosis with failing heart, etc.

5. Miscellaneous causes: (a) *Myxedema* is probably due to an accumulation of a semifluid albuminous substance in the tissue spaces. The method of accumulation is not definitely known; however, in experimental myxedema a high protein diet increases the edema, whereas a low protein-high carbohydrate diet increases it. This is thought to be due to an increased capillary permeability, permitting plasma to accumulate in the tissue spaces. A high protein diet would simply increase the intercellular osmotic pressure, attracting more water into the intercellular spaces. (See Chapter 22.) (b) *Hyperthyroidism.* Edema may result from the vasodilation and associated high systolic blood pressure. It may, however, be due to a hypoproteinemia which results from the enormous demands for food or thiamine chloride deficiency. A high protein diet with vitamin B complex improves the edema by increasing the osmotic index of the blood.

Atherosclerosis

Age and sex	60 years or over as a rule; male or female	Any age; male or female	Presenile, 35 to 40; usually men	Young—under 40, usually female	55 or over; male or female
Onset of symptoms and type of symptoms and signs	Gradual onset with *increasing pain; sensitivity to cold*; pallor, atrophy; absence of vasomotor response; coldness, numbness; bluish mottling; absence of pulsation in posterior tibial and dorsalis pedis; brown, purple, or black discoloration	Sudden agonizing *pain; muscles rigid;* foot and toes white, then blue, then black; no pulsation; saddle embolism may give symptoms in both legs	Pain, gradual onset; *passive congestion;* deep red or purple discoloration; ulcers about tips of toes or nails; infection common; no pulsation in post-tibial or dorsalis pedis; vasomotor response may be present	Slow—gradual atrophy *made worse in cold;* vasomotor response great; gradual atrophy of fingers, ulcers, and then gangrene; then secondary infection; pulse good	Rapid progress—red *infected area with* septic arthritis, osteomyelitis, cellulitis lymphangitis; slight pain; pulse absent in dry type may be present in wet or infected type
Laboratory aids, x-ray, etc.	High systolic diastolic, blood pressure; x-ray shows calcification .	X-ray negative	X-ray negative except atrophy of disease; low blood pressure	X-ray negative except atrophy	Blood sugar; urine; osteomyelitis shown by x-ray

TABLE IV

DIFFERENTIAL DIAGNOSIS OF COMMON VASCULAR DISEASE CAUSING GANGRENE OF THE EXTREMITIES—PERIPHERAL VASCULAR DISEASES

DISEASE	OBLITERATING ARTERIOSCLEROSIS	EMBOLISM	THROMBOANGIITIS OBLITERANS	RAYNAUD'S DISEASE	DIABETIC
Underlying morbid anatomy	Atherosclerosis (intimal); medial sclerosis (Mönckeberg); arterial tuberculosis	Atherosclerosis	Inflammatory with thrombus affecting arteries, veins, and including nerves; large or small vessels may be affected	Sustained vasospasm; perhaps dilation of deep pulmonary arch; finally sclerosis of vessels, fingers and toes	Lipoid deposits in middle coat of medium-sized arteries with calcification (Mönckeberg), also intimal thickening; frequently infected
Associated or causal diseases	Generalized arteriosclerosis; cause unknown (?)	Subacute bacterial endocardiac failure, auricular fibrillation, and mural thrombus in left auricle due to endocarditis	Erythromelalgia; phlebitis migrans	Syphilis; severe secondary anemia; acrocyanosis; emotional instability; sclerodactylia; scleroderma	Trauma to feet; surgery to toes; diabetes hard to control in presence of infection
Type and extent of gangrene	Dry; one or more toes, foot, sometimes lower leg	May involve lower leg or arm; wet often; dry rarely; obstruction higher than gangrene due to collaterals	Wet; toe or entire foot, arms and legs may be involved	Usually hands—both; rarely feet	Dry or wet; one or more toes or entire foot or leg
History	Nocturnal leg cramps; rarely intermittent claudication	The primary condition	Intermittent claudication; phlebitis migrans; heavy cigarette smoker; exacerbation in cold; remission in warm weather	Color changes—white, red, purple, then red	Usually some trauma or operation—otherwise no warning

Atherosclerosis

Age and sex	60 years or over as a rule; male or female	Any age; male or female	Presenile, 35 to 40; usually men	Young—under 40, usually female	35 or over; male or female
Onset of symptoms and type of symptoms and signs	Gradual onset with increasing pain; sensitivity to cold; pallor, atrophy; absence of vasomotor response; coldness, numbness; bluish mottling; absence of pulsation in posterior tibial and dorsalis pedis; *brown, purple, or* black discoloration	Sudden agonizing pain; muscles rigid; foot and toes white, then blue, then black; no pulsation; saddle embolism may give symptoms in both legs	Pain, gradual onset; passive congestion; deep red or purple discoloration; ulcers about tips of toes or nails; infection common; no pulsation in post-tibial or dorsalis pedis; vasomotor response may be present	Slow—gradual atrophy made worse in cold; vasomotor response great; gradual atrophy of fingers, ulcers, and then gangrene; then secondary infection; pulse good	Rapid progress—red infected area with septic arthritis, osteomyelitis, cellulitis lymphangitis; slight pain; pulse absent in dry type may be present in wet or infected type
Laboratory aids, x-ray, etc.	High systolic-diastolic, blood pressure; x-ray shows calcification	X-ray negative	X-ray negative except atrophy of disease; low blood pressure	X-ray negative except atrophy	Blood sugar; urine; osteomyelitis shown by x ray

Differential diagnosis of chronic lymphedema and chronic postphlebitic edema may be made on the following data:

In lymphedema there is very little disappearance of swelling on rest and elevation of the limb; in postphlebitic edema the patient usually reports a great reduction of swelling after a night's rest. In the former the superficial veins are normal; in the latter condition they are prominent and there is an increase in venous pressure. Ulceration and pigmentation of the skin is often present in the latter but not in the former and the swelling is soft and pitting in venous edema, whereas it is firm in lymphedema.

TABLE V

DIFFERENTIAL DIAGNOSIS OF CHRONIC LYMPHEDEMA AND CHRONIC POSTPHLEBITIC EDEMA
(After Barker and Allen: Proc. Staff Meet., Mayo Clin., 1940.)

IMPORTANT DIFFERENTIAL CONSIDERATIONS	LYMPHEDEMA*	POSTPHLEBITIC EDEMA†
Consistency of swelling	Brawny and firm	Soft; pits easily
Disappearance of swelling after elevation of limb	Slow and may be incomplete	Usually complete in 36 hours
Superficial veins	Normal	Usually prominent
Ulceration or pigmentation of skin; eczema; varicose veins	Always absent	May be present
Venous pressure	Normal	Increased

*May result from or be associated with cellulitis.
†May result from deep thrombophlebitis.

The differential diagnosis of acute cellulitis and acute thrombophlebitis are listed by Barker and Allen as shown in Table VI.

TABLE VI

DIFFERENTIAL DIAGNOSIS OF ACUTE CELLULITIS AND ACUTE THROMBOPHLEBITIS
(After Barker and Allen: Proc. Staff Meet., Mayo Clin., 1940.)

IMPORTANT DIFFERENTIAL CONSIDERATIONS	ACUTE THROMBOPHLEBITIS		ACUTE CELLULITIS
	SUPERFICIAL	DEEP (ILIOFEMORAL)	
Fever, temperature	Rarely exceeds 100° F. (37.7° C.)	Rarely exceeds 101° F. (38.3° C.)	As high as 106° F. (41.1° C.), unusually high
Chills	Absent	Absent	Frequent
Recurrence in same region	Uncommon	Uncommon	Common
Edema or enlargement	Absent	Common	Common
Evidence of venous congestion*	Usually absent	Common	Absent
Inflammation of skin	Linear, localized to vein	Absent	Size of palm of hand or more
Tenderness	Localized to involved vein	Localized to involved vein	Localized to region of inflammation
Palpable thrombosis of veins	Present	Usually absent	Absent

*Varices and prominence of superficial veins.

Treatment.—The treatment of edemas in the extremities will depend upon their cause. These discussions will be found under their respective headings throughout the book. Two examples may be cited.

If the obstruction is on the venous side, there will be an increase in hydrostatic pressure, causing edema. After the danger of dislodging a thrombus is over (four to six weeks), a tight bandage should be applied over the entire extremity. This increases the intercellular tissue pressure and the capillary blood pressure until it equals the tissue pressure. Filtration from the veins or into them cannot occur; however, since the osmotic pressure in the capillaries remains unchanged, fluid will be absorbed by the capillaries and lymphatics and ultimately the edema will be reduced. In addition, elevation of the extremity may be used to aid in its reduction.

The cause of swollen arms after radical breast operations is probably due in part to venous obstruction, although the lymphatic return may also be impaired. Homans and also Drinker and Fields have discussed the problem of lymphatic edema. They are of the opinion that it is very difficult to produce lymphedema experimentally or postoperatively by obstruction of the lymphatics alone. Homans believes that in phlegmasia alba dolens there is some lymphatic involvement with thrombophlebitis. The edema is due in part to the accumulation of protein material in the tissue spaces. The osmotic pressure in these spaces is increased, thereby preventing reabsorption of solutes and colloids by the blood capillaries. Increasing tissue space hydrostatic pressure by bandage forces proteins and crystalloids into the lymph capillaries. This stimulates the normal method of lymph movement, in which muscular contraction and arterial pulsation provide the only propelling force causing flow past the valves in the lymphatics. In the aged who are kept in bed for long periods of time, there is venous stasis (see Chapter 17). This is due to lack of the muscular activity upon which the venous return partially depends. Active motion tends to prevent this. Moreover, intermittent bandaging after mobilization of the patient may prevent the dependent edema which is caused by stasis when the patient resumes the upright position.

Intractable lymphedema which does not respond to conservative measures must be treated by plastic operations. These are done by turning back broad flaps which include the aponeurosis and which expose bone, muscles, and tendon sheaths. The operation includes one-half the circumference of the extremity. Then the lymph-soaked fibrous tissue and sclerosed fat are cut from the deep surface of the flaps which are left very thin. The other half of the operation may be done at a later date. This should be postponed for several months so that the flaps previously made will be healthy and withstand suturing of the new flaps. The first stage is usually anteromedial and the second stage is anterolateral.

The operation is done with a broad tourniquet so that a bloodless field is maintained. Communicating veins should be spared insofar as possible. The lateral sural branch of the common peroneal nerve should not be cut since it supplies the outer side of the foot and heel. At a later

time if the foot is still edematous, this can be treated in a similar manner at a third operation. Should the skin be ulcerated and infected, these operations must not be done because the flap will slough. Here it is better to excise large masses of tissue and then when granulations are healthy apply split-thickness grafts. Should the above measures fail, amputation must be done.

GANGRENE OF INFECTIOUS ORIGIN

1. Gas gangrene is discussed elsewhere (see Chapter 4). The bacterial toxin destroys wide areas of tissue and the effect is aggravated by the devitalizing effects of gas.

Since gas-producing anaerobes are normally present in muscles, the fact that there is crepitation does not mean impending gangrene. Very often air is absorbed without any clinical symptoms. In all severe injuries the wound should be cleaned, débridement done, and the wound left open. Tourniquets should not be used. By decreasing

Fig. 54.—Gas gangrene of the hand and forearm.

the oxygen supply they favor the growth of anaerobes. Should crepitation develop, this must be carefully observed. If there are no local spreading and no general symptoms, it will subside. X-ray treatment has been advocated by some. However, its remedial effects have not been definitely established. Gas gangrene is probably due to anaerobic bacilli and streptococci in symbiosis. Therefore sulfanilamide is helpful. In all badly contaminated accidental wounds polyvalent antitoxin of the gas bacilli group should be given, together with tetanus antitoxin, even if tetanus toxoid has been given, as a prophylactic measure. *Experimental wounds inoculated with clostridium welchii, Cl. septicum, Cl. novyi, or Cl. sordellii* caused death in guinea pigs within twenty-six hours. When inoculated with ten times the lethal dose and when at the same time sulfathiazole was introduced into the wound, 97 per cent recovered. Although various other experimenters have not obtained such results, there seems to be good evidence for the use of the sulfonamides locally. However, their effectiveness is probably dependent upon the local flora of bacteria in the infected tissues in addition to anaerobic gas bacteria. There are apt to be streptococci of the aerobic variety which use up the oxygen in the wound, producing an *anaerobic* medium. The local irritating effects of the sulfonamides would not be helpful. Penicillin is far preferable and should be used locally and parenterally in large doses.

Small wounds should be opened widely. Oxygen should be given by inhalation and a sterilized tube may be placed under the dressing which is attached to an oxygen tank, thus supplying the wound with oxygen directly. Wide incisions into the crepitant tissue with the foregoing treatment may save life and the extremity if instituted early. Should signs of septicemia appear or should the infection continue to spread, then amputation must be done promptly. Preliminary treatment with ice for a short period is indicated (q.v.). The amputation is done without flaps; that is, the "chop" or guillotine type is done. The stump is left wide open. Subsequently the stump may be surgically improved or flaps may be formed by stretching the skin with weights, or skin grafts may be used.

2. Phlegmon, or diffuse cellulitis, is also characterized by a toxemia and by wide destruction of tissue. This condition has been discussed in Chapter 4.

3. Hospital gangrene (phagedena or wound diphtheria) is very rare now. It may be due to the streptococcus or to a symbiotic growth of bacteria. Higher diphtheroids closely resembling the Klebs-Loeffler group may cause ulcers of the legs. Diphtheria antitoxin is specific for wound diphtheria—not for the diphtheroid.

Fig. 55.—Gas gangrene of the leg. The upper large granulating area was opened surgically. The lower one is the site of the injury. Gas in the tissues could be felt and was demonstrated by x-ray. The cellulocutaneous type of erysipelas resembles this lesion in the undermining of the skin. The wound was irrigated with hydrogen peroxide, and gas bacillus antitoxin given. The patient recovered.

4. Noma, cancrum oris, or gangrenous stomatitis is due to a mixed infection in the mouth. No doubt the devastating streptococcus is usually the causative organism. Since it occurs in debilitated children after scarlet fever or measles or in the early stages of leucemia, it is probably the "soil rather than the seed" that is at fault. It results in large sloughs of the cheek, with resulting high mortality. Trauma in the mouth by tooth extractions, etc., is contraindicated in such children. A similar condition rarely occurs about the genitals—noma pudendi.

The treatment of gangrenous stomatitis is repeated blood transfusion, adequate food and fluid intake, and sulfonamides, penicillin, and streptomycin. Locally surgery is contraindicated. A mouthwash of normal saline may be used but no strong antiseptics.

5. Ulcers due to specific organisms occur in mycotic infections and in tuberculosis, syphilis, chancroid, etc. *Mycotic infections*, lympho-

A. B.

Fig. 56.—*A*. Photomicrograph of muscle tissue infected with the Welch bacillus. Note the organisms and the destruction and separation of the muscles. *B*. Cross section of muscles, showing separation by gas.

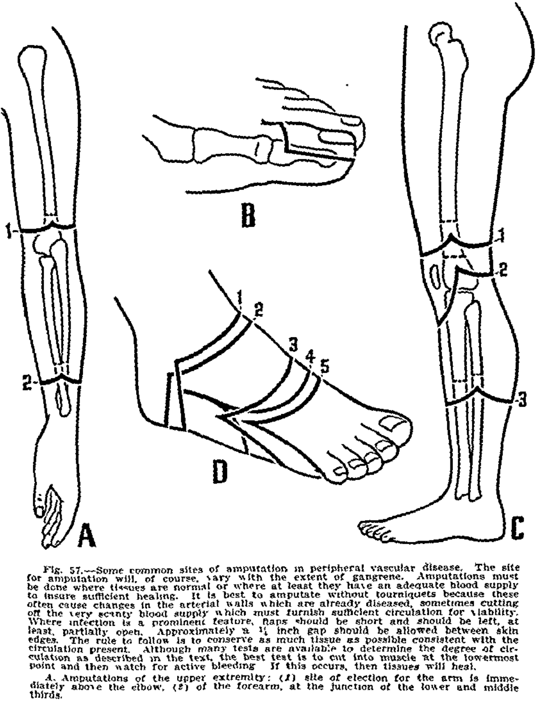

Fig. 57.—Some common sites of amputation in peripheral vascular disease. The site for amputation will, of course, vary with the extent of gangrene. Amputations must be done where tissues are normal or where at least they have an adequate blood supply to insure sufficient healing. It is best to amputate without tourniquets because these often cause changes in the arterial walls which are already diseased, sometimes cutting off the very scanty blood supply which must furnish sufficient circulation for viability. Where infection is a prominent feature, flaps should be short and should be left, at least, partially open. Approximately a ½ inch gap should be allowed between skin edges. The rule to follow is to conserve as much tissue as possible consistent with the circulation present. Although many tests are available to determine the degree of circulation as described in the text, the best test is to cut into muscle at the lowermost point and then watch for active bleeding. If this occurs, then tissues will heal.

A. Amputations of the upper extremity: *(1)* site of election for the arm is immediately above the elbow, *(2)* of the forearm, at the junction of the lower and middle thirds.

B. Lines of incision for amputation of the great toe.

C. Amputations of the lower extremity: *(1)* site of election at junction of lower and middle thirds (about 20 cm below the perineum), or just above the condyles; *(2)* the Gritti-Stokes amputation is slightly below the knee and conserves the patella for weight bearing; *(3)* below the knee amputations are best done at the junction of the upper and middle thirds, about 15 cm below the bend of the knee), and the fibula is divided at a higher level than the tibia.

D. Amputations through the foot: *(1)* Pirogoff; *(2)* Syme, *(3)* Chopart; *(4)* subastragaloid; *(5)* Lisfranc. These amputations will find few indications in peripheral vascular disease. Occasionally, however, they may be used.

Fig. 58.—Noma, cancrum oris, or gangrenous stomatitis.

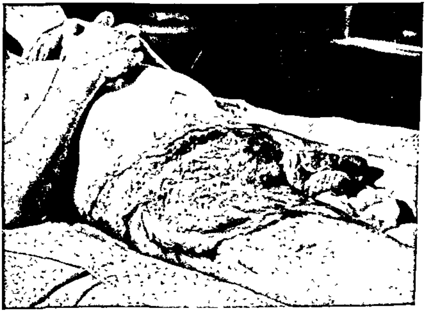

Fig. 59.—Spreading gangrene of the abdominal wall in a debilitated elderly man, following cecostomy.

granuloma inguinale, and granuloma inguinale are discussed in Chapter 7. They are extremely difficult to cure unless they are diagnosed early and excised. *Tuberculous* ulcers heal if and when the infection is arrested. *Syphilitic* ulcers *respond well to mixed treatment.* Exact diagnosis in ulcer of infectious origin may not be possible without the aid of the laboratory (smears, serological test, and biopsy).

6. Symbiotic gangrene is perhaps not an entity since most infections producing gangrene are combinations of organisms. Specifically the term has been used in streptococcus-staphylococcus infections producing widespread destruction of tissue. These are discussed in Chapter 4.

NEUROPATHIC ULCERS

Mal perforant is a painless ulcer on the heel.

Corneal ulcer after removal of the Gasserian ganglion for tic douloureux is neuropathic, as are also the ulcers on the extremities in tabes dorsalis. Does the ulcer develop because of a trophic disturbance to the part or because of anesthesia? This question is difficult to answer. If there is no feeling, repeated injury will remain unrecognized, permitting an ulcer to form. Syringomyelia and tabes dorsalis are diseases which may be complicated by ulcers of this type.

Peptic ulcer has been thought by some to be neuropathic in origin; indeed there seems to be ample ground for this hypothesis (Chapter 20).

MALIGNANT ULCER

As we shall learn in Chapter 15, a sore that does not heal is apt to be carcinomatous. On the lower lip we see squamous-cell carcinoma; on the face, basal-cell carcinoma; and in old, burned areas, Marjolin's ulcer, a form of squamous-cell carcinoma. The diagnosis is not difficult but may be made conclusive by biopsy. The treatment is excision or destruction by radium and x-ray.

ULCERS ASSOCIATED WITH SPLENOMEGALY

Such diseases as sickle-cell anemia, splenic neutropenia, Banti's syndrome, and hemolytic (spherocytic-acholuric) jaundice may be directly related to intractable ulcers of the lower legs. The cause of this mysterious combination is not known. No specific organisms are involved, and all local factors may be normal. After splenectomy the ulcers heal without specific therapy in most instances. (See Chapter 22.)

DISTURBANCES OF FAT METABOLISM

Fat is not altogether connective tissue with fat cells. It is perhaps an organ possessing in part some glandular function (Chapter 16). Local areas of fat necrosis (lipogranuloma) are observed in the breast and abdominal wall as well as in the omentum and other areas. The reaction

induced by mild or severe trauma may resemble carcinoma clinically but not microscopically where a focus of dead fat is seen surrounded by granulation tissue rich in fibroblasts and resembling a sarcoma. The area should be excised. Fat necrosis associated with acute hemorrhagic pancreatitis occurs in the abdomen. Here the death of fat is accompanied by splitting into fatty acid and glycerol. The glycerol combines with calcium to form a soap.

Lipophage granulomas (Darier sarcoid, erythema induratum—Bazin) may be tuberculids or tuberculosis in fat. Treatment is ill-defined and usually ineffective. Rest and attention to the general condition of the patient are usual measures. Penicillin and streptomycin are now being tried.

Relapsing febrile nodular nonsuppurative panniculitis (Weber-Christian's disease) is a skin disease of unknown etiology. Its name is descriptive of the clinical manifestations. Biopsies help establish the diagnosis. Penicillin is helpful; however, natural remissions occur.

Necrobiosis lipoidica diabeticorum is a cutaneous disease occurring on one or both legs. The lesions are flat, red papules with a yellowish corium containing lipoids and swollen collagen fibers. Treatment consists of insulin for the diabetes, a low fat diet, rest, and light x-ray exposure.

COMBINATIONS

Ulcers occur in many diseases without discovered cause and effect. For example, ulcer of the tongue in syphilis is frequently due to carcinoma. Leprosy and neuropathic ulcers are commonly associated. The many other combinations outlined in this chapter, while not all-inclusive, will give the surgeon an idea of the most common causes of peripheral ulcers and gangrene. In every instance the local lesion should be subjected to biopsy and a careful examination of the patient made.

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induced by mild or severe trauma may resemble carcinoma clinically but not microscopically where a focus of dead fat is seen surrounded by granulation tissue rich in fibroblasts and resembling a sarcoma. The area should be excised. Fat necrosis associated with acute hemorrhagic pancreatitis occurs in the abdomen. Here the death of fat is accompanied by splitting into fatty acid and glycerol. The glycerol combines with calcium to form a soap.

Lipophage granulomas (Darier sarcoid, erythema induratum—Bazin) may be tuberculids or tuberculosis in fat. Treatment is ill-defined and usually ineffective. Rest and attention to the general condition of the patient are usual measures. Penicillin and streptomycin are now being tried.

Relapsing febrile nodular nonsuppurative panniculitis (Weber-Christian's disease) is a skin disease of unknown etiology. Its name is descriptive of the clinical manifestations. Biopsies help establish the diagnosis. Penicillin is helpful; however, natural remissions occur.

Necrobiosis lipoidica diabeticorum is a cutaneous disease occurring on one or both legs. The lesions are flat, red papules with a yellowish corium containing lipoids and swollen collagen fibers. Treatment consists of insulin for the diabetes, a low fat diet, rest, and light x-ray exposure.

COMBINATIONS

Ulcers occur in many diseases without discovered cause and effect. For example, ulcer of the tongue in syphilis is frequently due to carcinoma. Leprosy and neuropathic ulcers are commonly associated. The many other combinations outlined in this chapter, while not all-inclusive, will give the surgeon an idea of the most common causes of peripheral ulcers and gangrene. In every instance the local lesion should be subjected to biopsy and a careful examination of the patient made.

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Chapter 7

MISCELLANEOUS INFECTIONS

Tetanus.—Tetanus is a disease caused by the bacillus of tetanus (*Clostridium tetani*), a rod-shaped, spore-forming bacillus which lives in an anaerobic environment. The spores assume the shape of small carpet tacks and are very resistant. They are found principally in animal excreta and gain entrance into the body through punctured or other wounds which seal themselves off, excluding air. *Clostridium tetani* are found in lacerated wounds, animal bites, and sometimes after operations on gangrenous extremities. A few cases have been reported after "clean" surgery in which the suture material was thought to be the source of the infection. The presence of spores of *Clostridium tetani* in a sterile wound will not cause tetanus, for the organisms multiply in necrotic tissue in the presence of concomitant infection. In this favorable medium the bacilli grow, liberating a water-soluble substance that diffuses through the adjacent skeletal muscles and acts on the neuromuscular end organs to cause a state of maintained contraction. Some of the exotoxin is absorbed by the blood capillaries and lymphatics.

Firor states that the symptoms of tetanus are due to absorption of the toxin by the lymphatics and capillaries. It then affects the motor end plates, initiating tonic but not clonic spasms of the muscles. Life or death depends on the amount of "altered" or lethal toxin in the spinal cord. The convulsions (clonic contractions) of tetanus are of central origin, whereas the rigidity (tonic spasm) of tetanus is entirely due to the action of the toxin on the neuromuscular end organs. Minute quantities of tetanus toxin, introduced directly into the anterior horn cells of the lumbar cord in dogs, produce severe clonic spasms but no rigidity. These animals die without any other evidence of tetanus although the dose is sublethal. Transection of the cord does not prevent the passage of the toxin from the nonvital portion of the spinal cord to the vital centers of the medulla. Division of all distal roots stops convulsive movements in the hindquarters but does not prevent death. Neutralizing doses of antitoxin (1,000 units or more) given intravenously before making spinal injections do not prevent death—even though free antitoxin is circulating in the blood at the time of death. Firor believes as a result of these experiments that tetanus toxin is altered in the cord to form a lethal toxin which is not neutralized by antitoxin, even if a million neutralizing doses are used. Tetanus toxin is not the only example of stepped-up virulence which may occur within the body although this seems paradoxical in view of the body's defense mechanisms. There is some evidence that in diphtheria a toxono is stepped up which affects muscles. An exotoxin can do this but not an endotoxin because the bacteria are taken out by the reticulo-endothelial system. Cross-circulation experiments further substantiate this hypothesis, for the recipient dog dies shortly after the donor dog develops convulsions. Both die of respiratory failure. If antitoxin is used before a lethal quantity of toxin is fixed in the spinal cord, the animal may be saved—even after symptoms of tetanus have developed. Tetanus is, then, a disease involving (1) muscles, affecting those muscles which have the best blood supply

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toxoid. Two injections of 1 c.c. of the combined toxoids are given three to four months apart. Very few reactions occur. Then, should exposure occur, a third dose of the tetanus toxoid is administered, protecting the patient in the emergency and perhaps for one to two years. However, another activating dose may be given when needed. Toxoid is made from bacterial toxins plus formalin incubated at 37° for thirty days. This gives rise to a nontoxic antigen or toxoid.

Experiences in the French army have shown the value of tetanus toxoid. Three injections of 1 c.c. each are given at monthly intervals. The U. S. Army circular advises an initial dose of toxoid (1 c.c.) administered subcutaneously on three occasions three to four weeks apart. A stimulating dose of 1 c.c. is given (a) at the end of one year, (b) before going to the theater of war, and (c) on receiving a wound. The British army in some echelons have also given tetanus antitoxin when a soldier is wounded. There is good evidence to show that the antitoxin may inhibit the antigenic action of toxoid for a period of two to four weeks; therefore the advisability of using the antitoxin with toxoid is questionable.

Should the disease occur, the treatment is again a thorough cleaning up of the source of infection after preliminary injection of antitoxin about the wound and then the administration of daily doses of tetanus antitoxin, intravenously, intramuscularly, and subcutaneously. Some observers insist that antitoxin should be given intrathecally through cisternal or lumbar puncture or both. Others aver that it may contribute to a fatal outcome by causing excitement, serum meningitis, and possibly cerebral or medullary edema. Perhaps the preservatives used in antitoxin are the irritating factor. We do not use tetanus antitoxin intrathecally. Concerning the administration of antitoxin, the rule is to give "enough."

The *treatment* of tetanus, according to Frior, consists in (1) injection of tetanus antitoxin (30,000 to 40,000 units) around the wound, to prevent dissemination of the toxin, (2) careful cleansing of the wound and drainage one half hour after the above injection, (3) the injection of an additional 70,000 units of antitoxin intravenously the first day, then daily intravenous injections of 5,000 units (because the antitoxin is rapidly destroyed in the body, eight to ten days), (4) either in oil per rectum to control convulsions, and (5) the use of artificial means of respiration to resuscitate the patient should respiration stop. Barbiturates or morphine should not be used to control convulsions for both are respiratory depressants and in tetanus death is caused by respiratory failure.

For the control of convulsions, ether in oil, given rectally, is best. Recently curare has been suggested in doses of 0.010 Gm. per kilogram intramuscularly. This drug has been used to supplement gas anesthesia because of its relaxing effect. Its use in tetanus is still experimental. The patient should be put into a dark room from which noise is excluded, because external stimulation tends to produce convulsions. If the patient has had serum of any kind before, or if he is the victim of hay fever, asthma, or hives, it is well to give the *antitoxin at half-hour intervals.* In the presence of the disease this same routine is followed before larger doses (5,000 units) are injected at daily intervals. Penicillin and streptomycin

and are used the most (therefore, the masseters) and (2) central nervous system and medullary centers, causing clonic convulsions and death from respiratory failure. (The reason the diaphragm is not affected as early as the masseters is probably that it is not so well supplied with blood.)

It was formerly thought that the toxin ascended in the nerve sheaths or perineural lymphatics until it reached the motor cells of the cord, medulla, and brain. This seemed to explain the clinical observation that the longer the incubation period, the more mild the disease; and the further removed the lesion from the brain, the longer the incubation period and consequently the less severe the infection. It was thought that the early trismus (tetanic spasm of the jaw or masseter muscles) was due to the lower portion of the motor area's being affected first. Firor's explanations seem to disprove these concepts.

He found an insufficient amount of toxin in excised nerves of animals with tetanus to explain the disease and showed that even if the toxin is in the perineural and endoneural lymphatics there is no evidence that they communicate with the cerebrospinal fluid or cord.

Whatever the explanation, because of the early spasm of the muscles of mastication, the jaw is fixed; therefore the popular name lockjaw. Later, other muscles become affected causing generalized tonic and clonic convulsions.

Treatment.—It should be remembered that high fever ensues from toxemia, and, if the patient is not actively treated, death occurs from respiratory failure. The prognosis is not good when there are generalized convulsions because this means that the toxin has entered the spinal cord. The mortality is about 30 per cent after such symptoms have occurred. The *treatment* is chiefly prevention and consists of a thorough and complete cleaning out of wounds, if seen within the first six to eight hours as described in Chapter 16. If seen later than this, and if the possibility of tetanus is strong, then 10,000 units of tetanus antitoxin should be injected about the wound *before* the cleansing process is begun to prevent dissemination of the toxin.

The wound is cleaned an hour or so later by flushing with hydrogen peroxide so that more oxygen may reach it, removing any foreign body that may be present and leaving it open so that the air may have ready access to the field.

This description of the first phase of the treatment of tetanus is a particular application of a fundamental rule in the prevention and treatment of any septicemia or toxemia; namely, "If the acute focus can be eliminated, blood stream infections will not ccur or will usually be annihilated."

Second in importance is the administration of 5,000 units of tetanus antitoxin. This does not prevent the disease but ameliorates its severity. should it occur. Tetanus toxoid is available now which may solve the problem of tetanus. It is given early in childhood along with diptheria

head demand the Pasteur treatment, because one does not dare wait for symptoms in the animal. (5) It is not necessary that obvious wounds be inflicted. Saliva of an infected animal on any small wound or open sore may cause the disease. Therefore, nurses and physicians who come in contact with known rabid animals or patients should take the Pasteur treatment. (6) The immunity conferred by the treatment is said to last approximately six months. (7) There is no evidence that animals may carry *the disease without being infected; however, they are infectious for about* three to five days before symptoms occur. If the virus does not get to the nerves or does so only in minute amounts due to a bite through heavy clothing, the patient may not contract the disease—exclusive of treated cases, only one out of six people exposed to rabies get the disease. Local treatment by cauterizing agents such as nitric acid is advocated by most *authorities provided the wound is seen within a half hour. In experimental* animals 20 per cent soap solution used within thirty minutes protects more animals than nitric acid, tincture of iodine, or sulfanilamide.

Granuloma Inguinale.—Granuloma inguinale is believed to be caused by the so-called *Donovan bodies.* The term granuloma is applied to those infections which are characterized by a great amount of granulation tissue. They are usually chronic and may be nonspecific in origin. It is probably the time element (chronic) rather than any specific tendency of the organism that calls forth the response. The disease is said to be venereal in origin.

Symptoms and Signs.—Chronic progressive ulcerations about the genitals, rarely the face or mouth, with many draining sinuses. Not many general symptoms. The *diagnosis* is made by finding the rodlike *Donovan bodies* in large mononuclear cells from scrapings of the lesions.

Prognosis and Treatment.—The disease runs a chronic course but can be cured. The treatment is increasing daily doses of antimony and potassium tartrate (tartar emetic up to $\frac{1}{10}$ grain). Aureomycin has been used recently with promising results. The dose is 25 mg. per kilogram of body weight every twenty-four hours in five equal doses.

Lymphogranuloma Inguinale (Lymphogranuloma Venereum, Lymphopathia Venereum).—Esthiomene is the name given to the disease with swollen vulva. *The causative agent* is a filtrable virus known as the Frei *antigen. The disease is communicated by personal contact and is usually* venereal in origin.

Symptoms and Signs.—A small sore appears on the genitals and is followed by swollen lymph glands. These soon break down and discharge a white pus. The entire genital region becomes a mass of draining sinuses, with draining fistulas extending into the bladder or rectum. Strictures of the rectum are common. The *diagnosis* is made by biopsy which shows the absence of Donovan bodies and a fairly characteristic microscopic picture. The Frei-Hoffman skin test helps. The disease may resemble chronic ulcerative colitis and may rarely give a positive skin test.

are used to control concomitant infections in the wound and to prevent lung complications. They are especially useful in tetanus from wounds not accessible for débridement and wide open drainage, such as tetanus of the uterus from induced abortion.

Hydrophobia or Rabies.—The disease is caused by a filtrable virus or a toxin which affects the central nervous system. This produces small black areas in the brain called Negri bodies. The disease is transmitted by the saliva of infected animals, principally dogs, but rabbits, chickens, fox, squirrels, and others have been known to transmit the disease. Pathological changes are very meager except for the Negri bodies

Symptoms and Signs.—In the dog there are two types, the dumb and the furious. In the former, the dog is languid and semiparalyzed; he lies lazily around, drooling saliva. The furious is accompanied by irritability, restlessness, and a tendency to snap and bite other animals and people. The incubation period in the dog is three to six weeks or longer. The disease gets its name from the fact that there is a spasm of the laryngeal muscles whenever swallowing is attempted. This makes the animal seem to be afraid of water. The disease is invariably fatal. In man, the incubation period is three to six weeks, sometimes longer. The virus travels along the peripheral nerves; therefore, a bite in the leg would have a longer incubation period than one on the head. The symptoms in man are restlessness, pain in the region of the wound, difficulty in swallowing, and regurgitation of water through the nose when swallowing is attempted and, finally, increasing dyspnea, convulsions, coma, and death. The diagnosis is made by watching the dog. Once symptoms occur in man, the disease is also invariably fatal.

Tetanus causes no demonstrable pathological changes internally. *Rabies* is identified by the presence of Negri bodies and diffuse degenerative changes, with cellular infiltration in the cord, midbrain, medulla, and the basal nuclei.

Treatment.—The treatment consists entirely in prophylaxis because treatment is unavailing after symptoms appear. The following rules should be followed: (1) Whenever a dog bites an individual, the animal must be locked up or confined and observed for two weeks. If at the end of that time no symptoms occur, it is not necessary to give the Pasteur treatment to the patient. (2) If symptoms occur in the dog, he must *not* be killed. He should be sent to the veterinary or kept confined until death. The head should then be sent to the State Board of Health. Pasteur treatment is started as soon as symptoms occur in the animal. This consists of fourteen, or if the animal is known to be infected, twenty-one injections of antirabies virus, made from the spinal cords of infected rabbits. Since the length of such immunity is short, vaccination should be repeated if a second bite occurs later. (3) All stray dogs that bite may be infected; therefore, any person who is bitten by a stray dog that cannot be found should take the Pasteur treatment. (4) Any dogbites about the face or

head demand the Pasteur treatment, because one does not dare wait for symptoms in the animal. (5) It is not necessary that obvious wounds be inflicted. Saliva of an infected animal on any small wound or open sore may cause the disease. Therefore, nurses and physicians who come in contact with known rabid animals or patients should take the Pasteur treatment. (6) The immunity conferred by the treatment is said to last approximately six months. (7) There is no evidence that animals may carry the disease without being infected; however, they are infectious for about three to five days before symptoms occur. If the virus does not get to the nerves or does so only in minute amounts due to a bite through heavy clothing, the patient may not contract the disease—exclusive of treated cases, only one out of six people exposed to rabies get the disease. Local treatment by cauterizing agents such as nitric acid is advocated by most authorities provided the wound is seen within a half hour. In experimental animals 20 per cent soap solution used within thirty minutes protects more animals than nitric acid, tincture of iodine, or sulfanilamide.

Granuloma Inguinale.—Granuloma inguinale is believed to be caused by the so-called *Donovan bodies.* The term granuloma is applied to those *infections which are characterized by a great amount of granulation* tissue. They are usually chronic and may be nonspecific in origin. It is probably the time element (chronic) rather than any specific tendency of the organism that calls forth the response. The disease is said to be venereal in origin.

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Symptoms and Signs.—A small sore appears on the genitals and is followed by swollen lymph glands. These soon break down and discharge a white pus. The entire genital region becomes a mass of draining sinuses, with draining fistulas extending into the bladder or rectum. Strictures of the rectum are common. The *diagnosis* is made by biopsy which shows the absence of Donovan bodies and a fairly characteristic microscopic picture. The Frei-Hoffman skin test helps. The disease may resemble chronic ulcerative colitis and may rarely give a positive skin test.

Prognosis and Treatment.—The prognosis is not very good. Years are often required to cure this disease. If seen early, complete excision of the infected glands and dilation of the rectal stricture may be curative. Later, excision of the rectal stricture may be necessary. The latter is accomplished by first doing a colostomy; then the stricture is excised and end-to-end anastomosis is done. (See Chapter 20.) Some advise the intravenous injection of the Frei antigen. Sulfonamides, penicillin, and streptomycin have been used with only fair success and aureomycin with much better results.

Diphtheria.—The *causative agent* is the Klebs-Löffler bacillus or the diphtheria bacillus. The disease is contagious and is caused by contact with the organism.

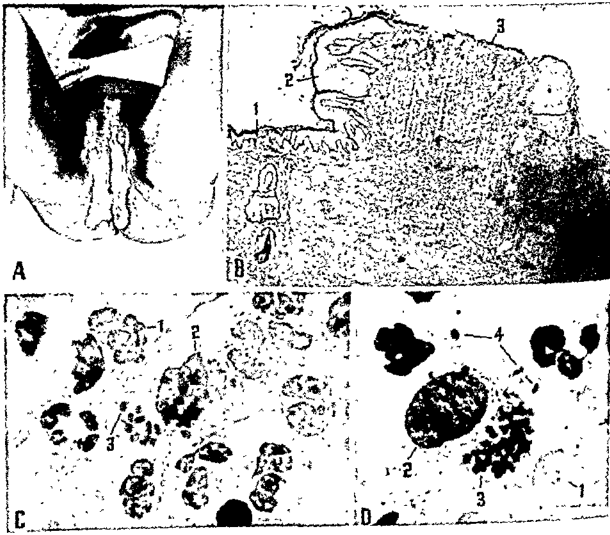

Fig. 60.—Granuloma inguinale. *A*. Clinical photo showing ulceration of vulva. *B*. Low power photomicrograph of edge of ulcer, *1*, normal skin, *2*, acanthotic epithelium; *3*, elevated edge of ulcer. *C*. Smears showing Donovan bodies: *1*, polymorphonuclear leucocytes, *2*, nucleus of large mononuclear cell, *3*, Donovan bodies in cell. *D*. Smear showing Donovan bodies: (*1*, red blood cell; *2*, nucleus of large mononuclear cell; *3*, Donovan bodies; *4*, extracellular Donovan bodies.

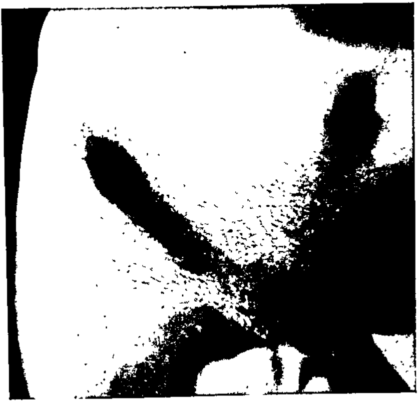

Fig. 61.—Lymphogranuloma inguinale, showing the enlarged inguinal nodes.

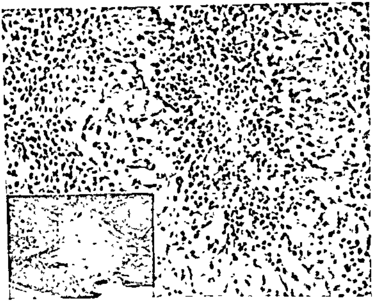

Fig. 62.—Lymphogranuloma inguinale. The low power shows extensive scarring of the lymph glands One of the surrounding lighter areas is seen in the high power. The nodule resembles a tubercle, it is surrounded by epithelioid cells. Its center, however, is filled with cells (lymphocytes and some polymorphonuclears) instead of caseous material. The necrotic material in these nodules is treated with phenol and heated to make the Frei antigen.

Symptoms and Signs.—The most common form is in the throat, where the germ produces a tough grayish pseudomembrane. There are marked general symptoms, with fever and malaise. We are interested here in the form which occurs in wounds, sometimes seen in nurses and physicians, causing a large slough which is covered by a pseudomembrane. Perhaps this was the "hospital gangrene" spoken of in the pre-Listerian days. The diagnosis is made by the clinical appearance and by the identification of the organism in smears and cultures from the wound. Identification is usually not easy.

Prognosis and Treatment.—The prognosis is good if treatment is promptly instituted.

Theoretically the disease should be extremely rare, which indeed it is in the author's experience. This is due to the widespread immunization against the disease (diphtheria toxoid). Should the disease occur, the treatment consists of large doses of diphtheria antitoxin. Local treatment consists of normal salt solution packs.

Yeastlike Fungus Infections.—These include blastomycosis, coccidioidal granuloma, torula infections, and histoplasmosis.

BLASTOMYCOSIS.—Blastomycosis is the chronic infectious disease of the skin, and occasionally of the lungs, caused by the yeastlike fungi *Blastomyces hominis* and *Coccidiodes immitis.* The fungus gains entrance through an injury or superficial wound and causes the development of small papules. Their development is extremely slow and the physician is apt to diagnose them as boils. Soon they break and discharge pus. This results in a widely indurated, bluish, hard area with multiple draining sinuses.

Diagnosis.—The diagnosis is made by finding the yeast fungus in the discharge, or better, in the biopsied tissue, which resembles tuberculous granulation tissue.

Treatment.—This consists of x-ray and the internal use of potassium iodide in increasing doses. The pulmonary form resembles tuberculosis. It is diagnosed by finding the fungus in the sputum. The iodides may help but this form of the disease is usually fatal. If seen early and diagnosed, excision of the lesions may result in cure.

COCCIDIOIDAL GRANULOMA (California Disease).—Coccidioidal granuloma is caused by the *Oidium coccidioides.* It is spherical and resembles the blastomyces but it multiples by the formation of endospores, whereas the blastomyces does so by budding. The disease resembles syphilis or tuberculosis clinically and microscopically. The lungs and other organs show calcification. Two chief varieties are seen: (1) the mild primary acute uncomplicated type called valley fever and (2) the chronic, highly fatal form which may affect any tissue or organ. Cattle, dogs, sheep, and other animals may harbor the fungus. Pus from the lesions may be injected into a male guinea pig; suppurative orchitis develops. There is no specific treatment.

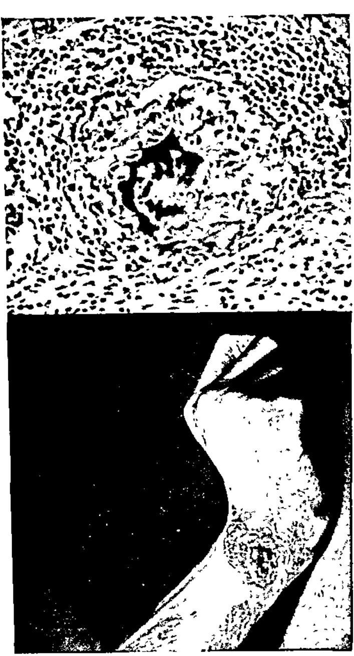

Fig. 63.—Blastomycosis. The chronic ulcerative lesion is shown. The photomicrograph shows the typical tissue reaction and the *Blastomyces*, with its double capsule. There are many fibroblasts, small mononuclears, and macrophage cells and some polymorphonuclears.

Symptoms and Signs.—The most common form is in the throat, where the germ produces a tough grayish pseudomembrane. There are marked general symptoms, with fever and malaise. We are interested here in the form which occurs in wounds, sometimes seen in nurses and physicians, causing a large slough which is covered by a pseudomembrane. Perhaps this was the "hospital gangrene" spoken of in the pre-Listerian days. The diagnosis is made by the clinical appearance and by the identification of the organism in smears and cultures from the wound. Identification is usually not easy.

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Theoretically the disease should be extremely rare, which indeed it is in the author's experience. This is due to the widespread immunization against the disease (diphtheria toxoid). Should the disease occur, the treatment consists of large doses of diphtheria antitoxin. Local treatment consists of normal salt solution packs.

Yeastlike Fungus Infections.—These include blastomycosis, coccidioidal granuloma, torula infections, and histoplasmosis.

Blastomycosis.—Blastomycosis is the chronic infectious disease of the skin, and occasionally of the lungs, caused by the yeastlike fungi *Blastomyces hominis* and *Coccidiodes immitis*. The fungus gains entrance through an injury or superficial wound and causes the development of small papules. Their development is extremely slow and the physician is apt to diagnose them as boils. Soon they break and discharge pus. This results in a widely indurated, bluish, hard area with multiple draining sinuses.

Diagnosis.—The diagnosis is made by finding the yeast fungus in the discharge, or better, in the biopsied tissue, which resembles tuberculous granulation tissue

Treatment.—This consists of x-ray and the internal use of potassium iodide in increasing doses. The pulmonary form resembles tuberculosis. It is diagnosed by finding the fungus in the sputum. The iodides may help but this form of the disease is usually fatal. If seen early and diagnosed, excision of the lesions may result in cure.

Coccidioidal Granuloma (California Disease).—Coccidioidal granuloma is caused by the *Oidium coccidioides*. It is spherical and resembles the blastomyces but it multiples by the formation of endospores, whereas the blastomyces does so by budding. The disease resembles syphilis or tuberculosis clinically and microscopically. The lungs and other organs show calcification. Two chief varieties are seen: (1) the mild primary acute uncomplicated type called valley fever and (2) the chronic, highly fatal form which may affect any tissue or organ. Cattle, dogs, sheep, and other animals may harbor the fungus. Pus from the lesions may be injected into a male guinea pig; suppurative orchitis develops. There is no specific treatment.

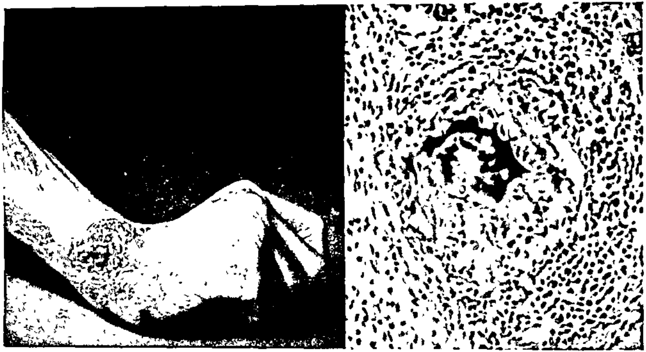


Fig. 63.—*Blastomycosis.* *The chronic ulcerative lesion is shown.* *The photomicrograph shows the typical tissue* reaction and the *Blastomyces,* with its double capsule. There are many fibroblasts, small mononuclears, and macrophage cells and some polymorphonuclears.

TORULA INFECTIONS.—Torula infections are caused by a yeast resembling the blastomyces. It may cause a meningo-encephalitis which is secondary to lung or other lesions.

HISTOPLASMOSIS.—Histoplasmosis (Darling) or reticulo-endothelial cytomycosis is caused by a yeastlike body, the *Histoplasma capsulatum.* The parasites occur in phagocytic cells as well as fixed reticulo-endothelial cells of the liver and spleen. They may be found in lymph nodes, bone

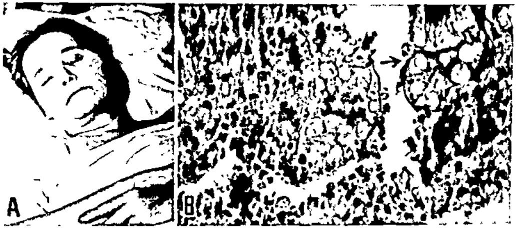


Fig. 64.—*A*. Clinical photograph of a patient with torulosis, showing swelling in parotid region. *B*. Abscess showing organisms in giant cells. Hematoxylin and eosin stain. The arrow points to a typical giant cell with organism

Fig. 65.—Histoplasmosis. Metamyelocyte showing histoplasma. *A*. Red blood cells. *B*. Nucleus of metamyelocyte. *C*. Spore.

marrow, and the peripheral blood. Clinically the disease may resemble kala-azar with fever, enlarged liver and spleen and lymph nodes, anemia, and leucopenia. There is great weakness and loss of weight. We have seen the disease in a child 3 years of age and in a man 70 years old. Biopsy of the lymph nodes or sternal puncture may reveal the organisms. It has been found in the stools. There is no satisfactory treatment for this

fatal disease. Recent studies have shown that the disease may appear in a mild form and that it is probably very common in many river valleys. Clinically the mild form of the disease resembles tuberculosis. The lungs and other organs show extensive calcification. Histoplasmin is used as a skin test and is interpreted much as the tuberculin test in making a diagnosis, although its reliability is questionable.

Actinomycosis.—Actinomycosis is another example of a fungus disease. It is caused by the *Actinomyces bovis* or ray fungus, a streptothrix which is a large, round organism with small bulblike threads extending around the periphery. As the fungus grows, it causes a slow but active *inflammation, with the formation of a large amount of granulation tissue,* particularly rich in macrophages, monocytes, and fibroblasts. (All diseases having this effect are called granulomas—tuberculosis, syphilis, and fungus infections). Soon secondary invaders enter the area and frank suppura*tion occurs. In the pus are small yellow grains called "sulfur granules."* The Actinomyces may be found in them or they may be composed of mycelia and parts of the organism. The infection ultimately produces extensive infiltration, which is seen clinically as a hard indurated area with *many draining sinuses, although the lymph glands are not involved.* In cattle the disease is called *lumpy jaw* because of the hard "lumps" that occur in the neck. It is said to occur in them from eating grains or grasses contaminated by the fungus. A slight abrasion in the mouth affords easy access. *In man two forms are seen: local and internal. The former* is usually in the head and in the neck and rarely in the skin elsewhere; the latter in the lungs, appendix, Fallopian tubes, and intestines, although any organ may be involved. The disease does not spread by the lymphatics *and therefore the lymph nodes are uninvolved. In this way it may* be distinguished from syphilis and tuberculosis. The spread is from the subcutaneous and submucous tissue by direct continuity. If a blood vessel is involved, the organism may be carried to any organ.

Diagnosis.—The diagnosis is made from the clinical signs (chronic inflammation with induration of tissues, very little pain and fever, absence of glandular involvement) and the laboratory tests. The internal forms show grossly a firm purulent mass of tissue which may resemble carcinoma. In the lungs multiple abscesses may occur. In the ileocecal region the picture may be that of a terminal ileitis. If some of the pus is put into a test tube of normal saline or weak sodium hydroxide, the sulfur granules may be seen. The final diagnosis is made by biopsy and identification of the fungus in tissue sections. Sometimes these organisms (probably benign types of Actinomyces) are found in the mouth or intestinal tract without symptoms. The outlook for the cutaneous form is reasonably good; that for the internal varieties, poor. On the face other lesions resembling Actinomyces must be thought of. The early lesion is usually thought to be a boil or carbuncle. Infected sebaceous cyst, osteomyelitis of the mandible with draining sinuses, anthrax, oriental sore (delhi boil),

Fig. 66.—Actinomycosis of the face in a boy aged 6 years. Great improvement resulted from x-ray treatment and the use of thymol internally.

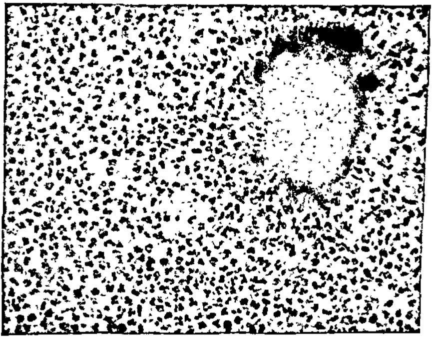
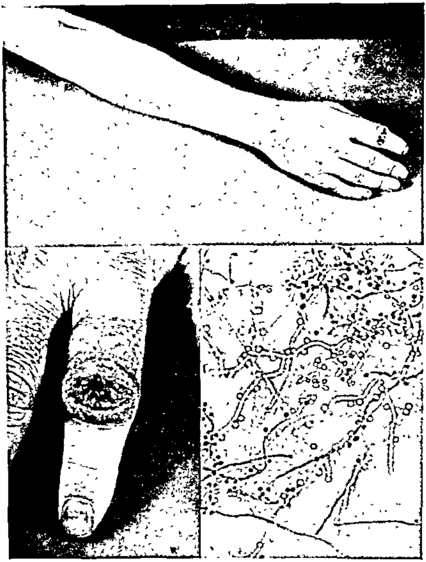


Fig. 67.—Actinomycosis. The photomicrograph shows the *Actinomyces*, or ray fungus. Note projecting mycelia. The fungus is surrounded by pus cells, many lymphocytes, fibroblasts, and macrophages.

carcinoma, and, in one case, an accidental smallpox vaccination have all been thought to be Actinomyces.

Treatment.—The treatment consists of x-ray and increasing doses of sodium or potassium iodide, large doses of the sulfonamides and penicillin locally (5,000 units per cubic centimeter) as well as intramuscularly,

A.



B. C.

Fig. 68.—Sporotrichosis. *A.* Primary lesion and the involved lymphatics. *B.* Closer view of the ulcer. *C.* Photomicrograph of the Sporothrix (moist preparation from agar 5 days old), showing the conidia or asexual spores.

100,000 units every three hours. If the skin lesion is seen early, diagnosed, and excised, a complete cure may be effectuated. In the abdominal varieties, operation, with removal of the diseased organ if feasible, is perhaps the treatment of choice. Ordinarily the surgeon does not make the correct

Fig. 66.—Actinomycosis of the face in a boy aged 6 years. Great improvement resulted from x-ray treatment and the use of thymol internally.

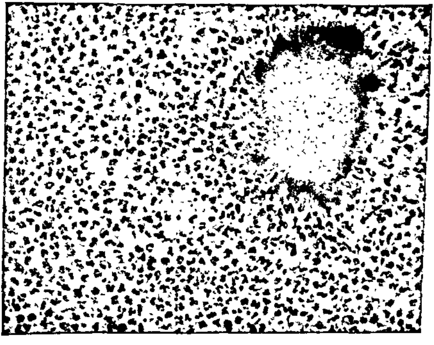


Fig. 67.—Actinomycosis. The photomicrograph shows the *Actinomyces*, or ray fungus. Note projecting mycelia. The fungus is surrounded by pus cells, many lymphocytes, fibroblasts, and macrophages.

giant cells. There is much necrosis. The disease is prevented by eating only cooked pork. There is no specific treatment. A skin test is available for diagnosis.

Staphylococcic Actinophytosis (Botryomycosis).—A mass of granulation tissue in a wound is ordinarily seen after healing by second intention. If it is removed and recurs, it may resemble carcinoma or fungus infection. *Pyogenic* granuloma is an excessive formation of granulation tissue caused by the staphylococcus. It has been called botryomyocosis or mycetoma because of its resemblance to such lesions in horses. The lesion contains granules which resemble the "sulphur granules" of actinomycosis. When crushed and stained with Gram stain, they are found to contain staphylococci. It is best treated by excision followed by x-ray.

Amebic Dysentery.—This is caused by the *Entamoeba histolytica*, a motile protozoon similar to the ameba we see in stagnant water. It is taken into the body in infected food or drink. It is extremely common in tropical countries, where carriers transmit the disease without themselves having symptoms. The amebae produce widespread ulceration in the colon and, rarely, in the small intestine. They do this by penetrating the lumen of the glands and reaching the submucosa where they produce necrosis by a proteolytic ferment which they release. The mucosa over the necrotic area dies, causing sloughs with large ragged undermined edges. In addition, the portal capillaries occasionally carry the amebae to the liver, where an *amebic* abscess may develop. This is usually a large single abscess with ragged necrotic walls and a great destruction of tissue. The chief symptom of amebic dysentery is a persistent diarrhea, with mucus and blood in the watery or loose stools. There may be fifty or sixty stools a day, and sometimes enormous sloughs of the mucus membrane occur. Occasionally diarrhea is not a prominent feature and the first evidence of the disease is a pelvic, subphrenic, or liver abscess. The patient soon becomes weak, emaciated, dehydrated, and feeble. Death may occur within one to two weeks. The chronic type is much milder but the symptoms are the same. Should a liver abscess occur, there will be chills, fever, sweats, tenderness over the liver, and perhaps a subphrenic abscess as well.

Diagnosis.—The diagnosis depends upon the appearance of the local lesion as seen through the proctoscope and the presence of the organism in the stool. This may be obtained by warm normal salt enema, cathartic, or direct smear. The stool should be placed in a sealed jar and kept warm for the laboratory examination. The physician in making the differential diagnosis must think of other lesions causing diarrhea, such as:

1. Acute infectious diseases: (a) bacilliary dysentery, (b) typhoid fever, (c) paratyphoid, (d) cholera, and (e) trichinosis.
2. Acute noninfectious diseases: (a) poisonings (bichloride of mercury, arsenic and (b) uremia.
3. Chronic infectious lesions: (a) tuberculosis, (b) chronic ulcerative colitis, (c) regional enteritis, (d) lymphopathia venereum, and (e) syphilis.

diagnosis until smears have been made from the abscess which is usually found. Fistulae are apt to follow any abdominal surgical procedure in the presence of Actinomycosis (see Chapter 20).

Granulomatous Nocardiosis.—Granulomatous nocardiosis is a new fungus disease which is thought to be caused by an acid-fast organism of the family of Actinomycetacae, *Nocardia intracellularis* (Cuttino and McCabe). It is a granulomatous inflammation causing proliferation of reticulo-endothelial cells.

Sporotrichosis.—Sporotrichosis is caused by the *Sporothrix schenki*, which grows readily, forming many mycelian threads. It usually occurs on the hands and forearms, with formation of nodules and ulcers along the tubular lymphatics. The lymph nodes are not involved. The disease may be chronic and is treated by palliation locally and increasing doses of iodides. If the iodides are given early there is rapid regression of the disease. If seen very early, local excision is indicated. Diagnosis is made by finding the organism in smears, by culture on Sabouraud's medium, and by intradermal tests.

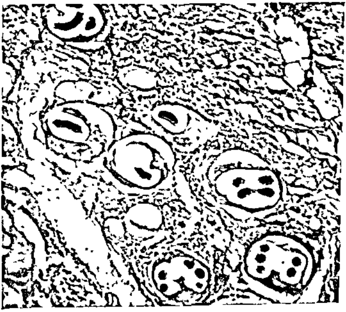


FIG. 69.—Trichinosis. Photomicrograph showing trichinae. Biopsy of skeletal muscle. The patient was a woman aged 21 years who complained of aching over the entire body and pain on motion of extremities. Her temperature was 103° F. and she was greatly emaciated. She had eaten raw pork two months before symptoms began.

Trichinosis.—Trichinosis is fairly common. It manifests itself by generalized muscular pain and tenderness over localized muscle areas. It is caused by the *Trichina spiralis*, a small parasite which walls itself in a capsule in the depth of the affected muscle. It is ingested by eating uncooked pork and is carried by the blood stream to any or all muscles but not to the brain or other organs. In the early stages the cysts are largely made of fat; later they become calcified. These parasites set up a marked inflammatory reaction, with lymphocytes, plasma cells, and foreign body

Anthrax.—Anthrax is an infectious disease caused by *Bacillus antracis*, a large gram-positive bacillus which gains entrance through an abrasion. It forms a pustular lesion, with great swelling and edema, which is accompanied by marked general symptoms. It is known as "malignant pustule" and is usually transmitted by unsterilized shaving or other brushes. It is seen in people handling wool, hides, or animal fur and is common in sheep and cattle. Three days after inoculation a red papule forms which develops into a large lesion with a necrotic center. Fatal pulmonary and intestinal types occur.

Diagnosis.—Diagnosis is made by finding the organism in smears.

Treatment.—The treatment consists of penicillin packs 5,000 units per cubic centimeter locally or bacitracin ointment and penicillin intramuscularly, 100,000 units every three hours.

Fig. 70.—Tularemia. The initial lesion is shown. The infection occurred after cleaning rabbits. The epitrochlear and axillary glands were enlarged. There was great systemic reaction, with chills and fever.

Glanders.—Glanders is also known as farcy. "Buds" and "pipes" appear, signifying involvement of the lymphatics. The disease is caused by *Bacillus mallei* and manifests itself as a rule by chronic indurated ulcers about the air passages Man has no immunity to it. There is a highly fatal pulmonary form. Diagnosis is by smears and discovery of the organism. Treatment is palliative. Vaccine (mallein) has been suggested. Streptomycin is effective.

Mycetoma Pedis (Madura Foot).—Mycetoma pedis is a chronic disease appearing usually in the lower leg and foot. Although the *Actinomyces streptothrix* is said to be the causative organism, the process is prob-

4. Chronic noninfectious lesions: (a) carcinoma, (b) strictures due to any causes such as just mentioned (tuberculosis, syphilis, lymphopathia venereum, regional enteritis, diverticulitis, carcinoma, trauma (such as injection of hemorrhoids followed by sloughs), (c) avitaminosis or deficiency diseases (pellagra sprue), (d) allergy, and (e) neuropathic causes.

5. Miscellaneous causes: pernicious anemia, hyperthyroidism, congestive heart failure, cirrhosis of the liver, leucemia, achylia gastrica, pancreatic disease, Addison's disease, and gastrocolic fistula after gastroenterectomy.

Treatment.—The treatment is by use of ipecac derivatives, such as emetine hydrochloride (0.065 Gm. doses), arsenicals, such as carbarsone (0.25 Gm. tablets) and acetarsone and Diodoquin (5, 7 diiodo-8-hydroxyquinoline) in 210 mg. doses. In chronic colitis, if a specific organism is not found, emetine as a therapeutic is indicated. Amebic abscess of the liver is best treated by emetine, carbasone, and aspiration. The abscess is usually sterile, for the organisms are in its wall and not in the reddish pus. Emetine may be injected into the cavity. Aspiration may be repeated at intervals. If secondary infection is present drainage may be necessary, but due to the high mortality of this procedure even here repeated aspiration should be tried first.

Tularemia.—Tularemia is an infection caused by the *Bacterium tularense* Pasteurella tularensis (after Tulare County, California). It is common in wild rabbits and is transmitted through slight skin abrasions to men who handle wild rabbits. It has come to be known as "rabbit fever" by the laity. The organism grows and produces an inflammation at the site of entrance. This is known as the initial lesion. From here it spreads along the tubular lymphatics, producing a lymphangitis with multiple small abscesses along its path (similar to those seen in sporotrichosis, a fungus infection) and lymphadenitis. There is also a pulmonary form with symptoms resembling pneumonia.

Diagnosis.—The diagnosis is made from a history of handling wild rabbits while hunting or preparing them; also by skin and specific agglutination tests. Agglutinations in dilutions of 1/100 are significant. They remain positive for life due to some continued activity at the site of the lesion.

Treatment.—The disease may be prevented if those who handle rabbits will wear rubber gloves. Other animals (squirrels) have been known to transmit the malady. After the infection is present, treatment is symptomatic, but specific Foshay serum may be tried. The disease is extremely slow in its evolution and cure but it is not often fatal. (The mortality is less than 4 per cent). Repeated blood transfusions are of great value. Streptomycin and Chloromycetin have been used with success.

Four types of tularemia are seen: (1) *Ulceroglandular* (primary lesion and ulceration along lymphatics), (2) *oculoglandular* (primary lesion in the conjunctiva), (3) *glandular* (no local lesion but involvement of the lymph glands), (4), *typhoid type* (resembling typhoid fever).

is no specific treatment. Penicillin and Chloromycetin may be tried. Amputation may be necessary.

Leishmaniasis.—Visceral leishmaniasis, kala-azar, infantile kala-azar, and "death fever" are produced by *Leishmania donovani.* The organism belongs to the protozoa and is usually found in monocytes, reticulo-endothelial cells, and polymorphonuclears. It is round or oval and has an eccentric nucleus and another rodlike chromatin body. Within Wright's stain the protoplasm is light blue with pink nucleus and violet rodlike body. The principal lesions are observed in the spleen (tropical splenomegaly), liver, bone marrow, heart, kidneys, and lymph nodes. The entire reticuloendothelial system, including the free histiocytes, becomes parasitized, producing anemia, leucoplenia, splenomegaly, and enlargement of lymph nodes. The symptoms are chills, fever of an irregular type, edema of the skin with ulcers and hemorrhages, diarrhea, and extreme emaciation. There is no ascites as in intestinal schistosomiasis.

Diagnosis.—The diagnosis is established by finding the *Leishmania donovani* in smears from the peripheral blood, splenic pulp, lymph nodes, or bone marrow.

Treatment.—Treatment is usually with sodium or potassium antimony tartrate. A 2 per cent solution is freshly prepared and in the adult 2 to 5 c.c. are given intravenously every other day until 4 Gm. of the salt have been given. A newer drug is sodium antimony biscatechol disulphonate (Fuadin).

CUTANEOUS LEISHMANIASIS (ORIENTAL SORE, ALEPPO BUTTON, JERICK'S BOIL, DELHI BOIL).—Cutaneous leishmaniasis is caused by *Leishmania tropica.* It is transmitted by the sand fly, *Phlebotomus papatasii.* The disease is characterized by a red papule which later ulcerates. The lesions may occur on the face (most common), lips, hands, or feet. Treatment consists of intramuscular injections of Fuadin, 0.5 c.c. for children and up to 5 c.c. for adults.

MUCOCUTANEOUS LEISHMANIASIS (ESPUNDIA, AMERICAN LEISHMANIASIS).—Mucocutaneous leishmaniasis is caused by *Leishmania braziliensis.* It begins with a sore on an exposed surface of the skin. Later the mucous membrane of the mouth, palate, pharynx and larynx become ulcerated. Treatment is the same in other forms of leishmaniasis.

Schistosomiasis.—This group is caused by digenetic trematodes known as blood flukes or human schistosomes. The organisms lay eggs in veins which are discharged in urine or feces. Eggs hatch in water, forming embryos which hatch and escape as free-swimming organisms. In coming in contact with the fresh water snail they infect it, multiply, and form cercariae which break out of the snail and burrow through the skin of human beings who are swimming or wading. The cycle is then repeated.

VESICAL SCHISTOSOMIASIS (SCHISTOSOMIASIS HEMATOBIA, VESICAL BLOOD FLUKE, SCHISTOSOMA HEMATOBIUM).—There are general *symptoms* of in-

ably conditioned by the growth of various fungi called mycetoma grains. Usually a nodule appears on the plantar surface of the foot. This is followed by others which finally become soft and break, causing multiple sinuses. There may be great destruction of the entire foot involving bones and joints. The clinical appearance resembles tuberculosis. Diagnosis is established by finding the fungus in the infected epidermis or in the pus. There

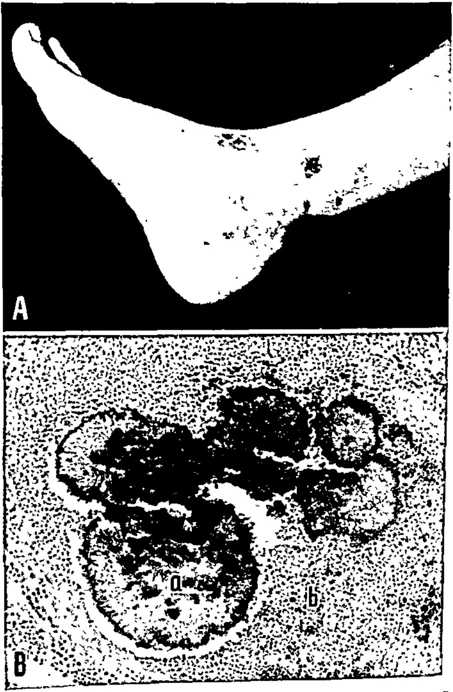


Fig. 71.—*A*, Clinical photograph showing madura foot with many sinuses. *B*, Colony of medura myces in an abscess of the foot (Graham-Weigert stain). *a*, Colony of spores; *b*, pus.

is no specific treatment. Penicillin and Chloromycetin may be tried. Amputation may be necessary.

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Vesical Schistosomiasis (Schistosomiasis Hematobia, Vesical Blood Fluke, Schistosoma Hematobium).—There are general *symptoms* of in-

fection and local bladder irritation. The diagnosis is established by recovering the organism. Treatment is with tartar emetic potassium antimony tartrate.

INTESTINAL SCHISTOSOMIASIS, SCHISTOSOMA MANSONI.—Intestinal Schistosomiasis is caused by *Schistosoma mansoni*. The symptoms are chiefly diarrhea with general malaise and fever. Later dysentery becomes less prominent but there are loose stools due to fibrous constrictions in the thickened bowel, anal fissures, and fistulae ovum. There may be pronounced splenomegaly or (Egyptian splenomegaly) hepatomegalia. The diagnosis rests upon finding the eggs of the organism. Treatment is with tartar emetic.

ORIENTAL SCHISTOSOMIASIS, SCHISTOSOMA JAPONICUM.—Oriental schistosomiasis is caused by the oriental blood fluke which also causes dysentery and splenohepatomegalia. The treatment is the same as for other types of schistosomiasis.

Echinococcus Disease.—Echinococcus disease or hydatid disease is caused by *Echinococcus granulosus, Echinococcus tenia,* or *Echinococcus multilocularis.* It is a tiny tapeworm which lives in the small bowel of the dog and other hosts. After excretion it may be ingested by intermediary hosts—sheep, hogs, cattle, or man. After the embryo is set loose it burrows out of the intestine and finally settles into the liver, lung, pleura, kidney, brain, and other organs. Here it forms cysts, daughter cysts, brood capsules, and scoleces.

Diagnosis.—The disease is considered as a possibility when cysts or cyst-like swellings are found by physical examination or x-ray study of organs in which symptoms occur. Aids to diagnosis are x-ray examination, the presence of eosinophilia of the organ or the portion involved, precipitin complement fixation, and intradermal tests.

Treatment.—Treatment consists of surgical excision if possible such as lobectomy in the lower lobe of the lung. If not, the cyst may be aspirated, care being taken not to spill any of its contents, thereby preventing secondary contamination and infection. Then 10 to 50 c.c. of 10 per cent formalin is injected and withdrawn after five minutes. Now the cyst is separated from its adventitia and removed. The adventitia is then swabbed with 10 per cent formalin, leaving a small amount. The cavity is then obliterated by suture and the wound closed without drainage. Marsupialization may also be used in conjunction with formalin treatment if secondary infection is present.

SUMMARY

In this chapter we have discussed some of the more common types of miscellaneous infections. There are many more which the surgeon sees, such as bacillary dysentery, Malta or undulant fever, bubonic plague, leprosy, mycosis; protozoan infections such as malaria, relapsing fever;

diseases caused by metazoan parasites, among which are filariasis; and lastly, diseases of partially known etiology, such as infectious jaundice, psittacosis, Rocky Mountain spotted fever or tick fever (caused by rickettsiae), ratbite fever, etc., diseases which are now treated with aureomycin or chloromycetin.

Diagnosis in these diseases is made by clinical observation and by routine and special laboratory tests.

Special laboratory tests are agglutination tests for Malta fever and tularemia, a special agglutination test (heterophile antigen, Paul-Bunnel) for infectious mononucleosis, agglutination with Proteus X19 for typhus (Weil-Felix reaction), search for spirochetes in the urine, and guinea pig inoculation in Weil's disease (spirochetosis icterohaemorrhagica), blood cultures in typhoid, etc.

Certain diseases have similar manifestations and must be ruled out. For example, a group of chronic drainage sinuses are seen in (1) infected wounds with foreign bodies, (2) tuberculosis, (3) syphilis, (4) fungus infections, and in (5) carcinoma or sarcoma. Another example is the group causing an enlarged spleen (splenomegaly), as in kala azar now treated successfully by ethylstibamine Neostibosan) malaria, and Echinococcus infestations. Sometimes the lead is very flimsy; perhaps the patient reveals a bit of important history which he considers irrelevant: a small transient rash, a vacation in another district where certain infections are prevalent, a slight nosebleed, a purpuric spot, a pain in the region of the spleen, etc.

Since the advent of World War II many diseases hitherto considered curiosities may become not uncommon.

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Chapter 8
TUBERCULOSIS

Tuberculosis (from tuberculum, a nodule is an infectious and contagious disease caused by the *Mycobacterium tuberculosis.* It is transmitted to susceptible individuals by contact with the germ, either by inhalation (human strain) or by ingestion (bovine strain, usually) and may affect any tissue or organ in the body. Although not primarily a surgical disease, the surgeon is frequently called upon to aid in its management. We should speak of the infection in tuberculosis as a *tuberculous,* not a *tubercular,* infection, for "tubercular" nodules occur in other diseases, such as fungus infections, leprosy, etc.

PATHOLOGICAL FEATURES

The "unit" of the disease is the *tubercle,* which forms when tubercle bacilli are carried to the tissues by the lymphatics, the blood stream, or even by macrophage cells.

Tubercle bacilli may be present in the mucous membrane of the throat, for example. Here the polymorphonuclear cells may ingest them as they would any foreign body. These cells are then carried by the lymphatics to the lymph nodes, where they are fixed. If the polymorphonuclears are injured, the macrophage engulfs both cell and bacteria. If not, bacteria proliferate and destroy the polymorphonuclear cell. In either event, the macrophages engulf them. Growth may also take place inside the macrophage cells. As soon as the bacteria proliferate, tissue cells are injured and a reaction takes place with slight hyperemia, exudation, and attraction of macrophages, epithelioid cells, and giant cells. Some believe this reaction is the same in primary and in secondary infection, except that in the former it is milder. Most observers agree that when the tubercle bacilli first enter the body and find lodgement in the tissues there is no allergy present. Therefore, there is no specific reaction on the part of the tissue. The focus of bacilli is challenged, as any other foreign body or nonspecific infection would be. The walling off process through cellular proliferation is almost complete before allergy can be detected. This reaction holds the tubercle bacilli in check quickly and completely in most cases. It is not due to natural or acquired immunity any more than the reaction to the staphylococcus when it is first met. The most susceptible (Negro, Mexican, Indian) meet it in the same way. After the initial infection, if the tubercle bacilli subsequently reach the tissues either from exogenous or endogenous sources, a specific reaction takes place due to allergy to the tuberculoprotein. Some suggest desensitization as a means of control. Thus we may conclude that (1) allergy in this disease can be produced only by infection with (living or dead) tubercle bacilli and (2) allergy accentuates and hastens the native tissue reactions against tubercle bacilli.

The reaction which is set up by the tissues is specific and more or less typical, especially if the patient has had previous experience with the disease. Whereas it may be difficult to distinguish the *primary infection*

from a nonspecific inflammation (tubercles are rare), yet this initial experience produces a sensitiveness (allergy) to the endotoxin which causes a second infection to form lesions of the *secondary or adult type* which are fairly characteristic of the disease.

In the so-called childhood type in the lungs, for example, the infection is usually in the base of the lung. There may be extensive involvement with perhaps only one (Ghon) tubercle. Some have explained the occurrence of the adult type in infants by endogenous sensitization through the mother.

From the tubercle the disease is spread by continuity of tissue by the blood stream, by the lymphatics, and by phagocytic cells to any and all parts of the body. The tubercle is formed as a result of the endotoxin in the tissues. It is nature's answer to the attack. At first there is a slow, "cold" necrosis, or formation of a cheesy mass, a process known as *caseation or homogeneous coagulation necrosis.*

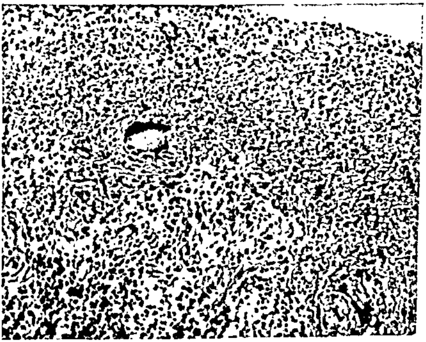

Fig. 72.—Tuberculous granulation tissue. Note the Langhans' type of giant cell and the epithelioid cells surrounding it.

Some pathologists regard caseation as the end result of coagulation necrosis, in which some cells are still recognizable.

Certain cells are now attracted to the area and they arrange themselves in a rather typical manner. There is a central giant cell (Langhans' type) which is surrounded by the the caseous material. This in turn is surrounded by a special type of reticulo-endothelial cell known as an *epitheloid cell,* in palisade arrangement. These cells are important in the histological diagnosis of the disease even if caseation is not present. They come from wandering cells (macrophages) and may form fibroblasts which give rise ultimately to fibrous tissue. Many mononuclear leucocytes are

seen surrounding the area, and there is marked proliferation of fibrous tissue (from fibroblasts). The blood supply to a tuberculous nodule is very poor. Even the capillaries which were present at the onset are obliterated. Therefore, tuberculosis is comparable in its pathological appearance to an infarct. From this "unit" the disease may spread to contiguous tissues. The epithelioid cells, the mononuclears, and the delicate connective tissue undergo the same coagulation necrosis, which in turn produces a similar reaction. In this way many tubercles are joined together (conglomerate tubercle). Finally large areas may be involved and there may be erosion into a large vessel, causing hemorrhage. No tissue is immune to this destructive process.

The *method of spreading* is by (1) contiguity, (2) erosion, (3) erosion into a blood vessel with dissemination, (4) lymphatic invasion, and (5) normal channels, as by coughing up the infected sputum from the lungs and swallowing it, with resultant infection of the gastrointestinal tract.

TERMINATION

Perhaps a better understanding can be obtained of the various types of tissue reaction to the disease by comparing it with nonspecific infections, as is done in the accompanying outline. As was pointed out in Chapter 4, these reactions may vary in type and intensity, depending on the virulence of the organism and the resistance of the patient.

TABLE VII

NONSPECIFIC INFECTION	TUBERCULOUS INFECTION
Resolution	Resolution may and frequently does take place in the adult type and practically always does in the primary type
Necrosis with absorption	Coagulation necrosis (caseation): a small area may be absorbed
Necrosis and sloughing	Cavitation from coagulation necrosis and sloughing
Suppuration (hot)	Liquefaction (cold abscess)
Healing occurs by cicatrization	Fibrosis
	Calcification produces a permanent arrest of infection; while not pathognomonic of tuberculosis, it is most commonly seen as the end stage in this disease

Clinically three types of tuberculosis are usually designated: (1) Exudative—little or no fibrous tissue proliferation occurs and the disease frequently ends in resolution; (2) caseous or ulcerative—caseation occurs with destruction of tissue and cavitation; (3) fibrous, proliferative, or productive (that is, productive of fibrous tissue). One or all of these types may be present in the same organ or tissue.

METHODS OF DIAGNOSIS

A diagnosis of tuberculosis may be made in any of the following ways.

History.—There may be a history of intimate contact with the disease.

Clinical Signs and Symptoms.—There may be slight fever, loss of weight and appetite, and local symptoms and signs; if the lungs are involved, there may be cough, sputum, hemoptysis, etc.

Skin Tests.—Of these, the von Pirquet and Mantoux tests are the best. In the von Pirquet test old tuberculin is used on a skin scratch: an inflammatory reaction indicates a positive test. In the Mantoux test an intracutaneous injection is made: this will cause a skin reaction if positive. A positive test indicates that the individual is allergic to the endotoxin of the tubercle bacillus: as interpreted clinically, this means that the patient has or has had the primary infection. (An anergic reaction is one in which there is a delay in the appearance of allergy). These tests have been found to be positive in 10 to 30 per cent of all adults, with variations in different localities. Therefore, a positive test does not help much in the diagnosis, but a negative test means that the patient does not have tuberculosis (or else that the disease is overwhelming, or that it is obsolete because of complete calcification). In other words, live bacteria must be present and they must have access to the blood stream for the test to be positive. Complete calcification gives a negative test.

X-ray Examination.—X-ray pictures of the affected part will show characteristic lesions. Calcifications may be due to other causes (coccidioidal infections, histoplasmosis) than tuberculous.

Laboratory Tests.—(1) The sputum is examined for acid-fast bacilli —small rod-shaped organisms which stain with difficulty but which, when stained by a special technique, retain the stain even after treatment with acid. (2) A biopsy of the tissue is performed when possible and when positive reveals typical tuberculous granulation tissue, in which the tubercle bacillus may often be seen. (3) A susceptible animal (guinea pig) is inoculated with the sputum or exudate from doubtful cases and in the presence of the tubercle bacillus will develop unmistakable tuberculous lesions.

PROGNOSIS

The prognosis is good. There is no disease which tends to cure itself more readily than tuberculosis. Recovery is slow and involves care, but the infection will in most cases become arrested if the forces of nature are given a chance. Arrest is brought about by fibrosis, or perhaps, more permanently, by calcification. *The general treatment* consists of adequate rest, good food, and sunshine. Streptomycin is extremely useful in many forms of tuberculosis. Other drugs which may help are para-aminosalicylic acid (P.A.S.) and sulfonamides. The local treatment consists of excision or immobilization of the part affected. Rest is secured by conservative measures in children and by more radical measures in adults.

SPECIAL TYPES OF TUBERCULOSIS

Tuberculous Lymphadenitis

Tuberculous lymphadenitis may arise from infection in the blood stream or from a neighboring focus. In the former there may be generalized

involvement of all nodes. Usually the disease is limited to one group which are infected secondarily by the primary focus—the cervical nodes from the tonsils and adenoids, the tracheobronchial nodes from the air passages and lungs, the axillary from the breast or arm, the inguinal from the anus, rectum, and perineum, and the mesenteric from the lymphoid tissue of the ileum, cecum, or appendix. Often the primary site has healed or at least cannot be demonstrated. The cervical glands are most commonly involved. They soon break down and become matted together into a conglomerate mass which may undergo liquefaction. Sometimes a single fibrous node is seen, especially in elderly patients. The treatment is the general treatment for tuberculosis supplemented by the irradiation of the nodes with ultraviolet light or short x-ray exposures and streptomycin. Complete

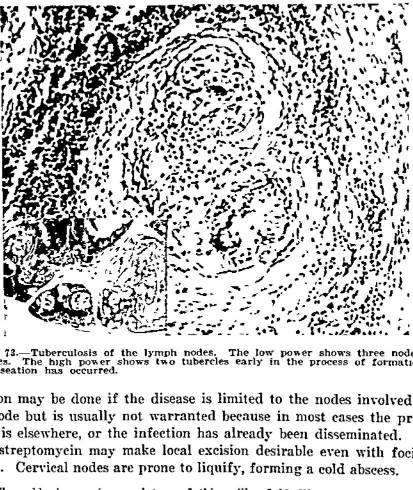

Fig. 73.—Tuberculosis of the lymph nodes. The low power shows three nodes with tubercles. The high power shows two tubercles early in the process of formation, before caseation has occurred.

excision may be done if the disease is limited to the nodes involved or to one node but is usually not warranted because in most cases the primary focus is elsewhere, or the infection has already been disseminated. However, streptomycin may make local excision desirable even with foci elsewhere. Cervical nodes are prone to liquify, forming a cold abscess.

The cold abscess (accumulation of thin milky fluid filled with lymphocytes) is said to contain Much's granules. These are fragments of tubercle bacilli which act as antigens in an unfavorable environment and may actually stimulate local immunity. When injected into sensitized or susceptible animals they may produce the disease. Rollier believes that psoas abscess has a favorable effect on tuberculous spondylitis (Pott's disease). The presence of immune bodies has not been demonstrated definitely in this liquefied material The danger is that of secondary infection, to which it seems to be poorly resistant.

Ordinarily a cold abscess should not be molested. In cases, however, where such an abscess is about to break as a result of pressure necrosis, or where there is secondary infection or *interference with function* (swallowing or breathing, or a rapid increase in size), the fluid may be *aspirated* through healthy tissue. This with streptomycin plus penicillin or sulfonamides, is usually sufficient. Should aspiration fail, and it often does, then incision with curettement of the gland or glands or their excision is indicated. If the primary foci are the tonsils, they should be removed. Small groups of nodes may be excised completely.

Tabes Mesenterica

Tabes mesenterica is tuberculosis of the mesenteric glands and is also usually due to bovine strains. The diagnosis is difficult but is often suspected. Two types of symptoms may occur. Those which arise from intestinal dysfunction (namely nausea, vomiting, flatulence, diarrhea) and those which give rise to pain resembling appendicitis. In both groups there is some fever and malaise. Leucocyte counts are low. These same symptoms are seen in nonspecific mesenteric lymphadenitis (Chapter 20) and diagnosis may be established only after operation and microscopic study of a lymph node.

Treatment.—*The only treatment* is the general care of tuberculosis, including streptomycin, unless there is interference with intestinal function or associated tuberculous peritonitis. Prognosis is good.

Tuberculous Peritonitis

Two clinical and pathological types are seen. (1) In the *ascitic* or *exudative* type, which occurs in young persons, the abdomen fills with clear fluid (ascites) and the intestines are studded with tubercles without demonstrable cause. (2) In the *fibrotic* or *fibrocaseous* (proliferative) type the intestines are matted by adhesions and areas of caseation are found. Sometimes both types are present simultaneously.

Some regard the fibrocaseous type as the late stage of the exudative type.

The portal of entry is said to be in the Fallopian tubes in girls and in the appendix in boys. However, the mesenteric nodes, spleen, and intestines may act as foci. It is perhaps best to regard most cases as hematogenous in origin. Simple exploration and exposure to air sometimes effectuates a cure.

The reason for the beneficial effect of laparotomy in exudative tuberculous peritonitis is not entirely clear. It may be due to the intestinal splinting following laparotomy, to the presence of air (some advocate pneumoperitoneum by air injection as good treatment, just as is done in pneumothorax), or to the reactive hyperemia that is set up, with attraction of phagocytic cells.

In the first type the appendix and/or the tubes may be removed. In the second type this is sometimes necessary, but is apt to be followed by intestinal fistulas.

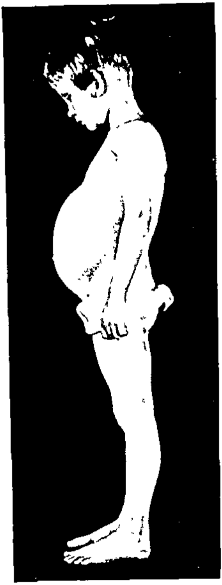

Fig. 74.—Tuberculous peritonitis, with ascites.

Tuberculosis of the Intestines

Tuberculosis of the intestines is also commonly caused by the bovine strain, although the human strain frequently causes a tuberculous enteritis. A chronic type attacks the lymphoid tissue of the ileum (tuberculosis affects lymphoid tissues throughout the body). Due to the fact that tuberculosis spreads along the lymphatics and that in the intestine the lymphatics encircle the bowel, the ulcers that form are known as *girdle ulcers,* in contrast to typhoid ulcers which spread in Peyer's patches with the long axis of the bowel. These contract and produce symptoms of bowel obstruction. Frequently the tuberculous mass is very large and can be felt at the ileocecal valve (where the lymphoid tissue is abundant).

The disease in this region may thus be of three types: (1) Ulceration of the ileum or cecum with or without perforation, (2) hyperplastic ileocecal tuberculosis, or (3) tuberculosis lymphadenitis. All types respond well to streptomycin therapy unless irreversible changes have occurred. The ulcerative type may require surgery to relieve intestinal obstruction due to fibrosis. Here a short-circuiting operation or resection is indicated. Hypertrophic ileocecal tuberculosis requires resection of the terminal ileum, cecum, and ascending colon with ileotransverse colostomy if feasible. If not, a sidetracking operation may be done. Glandular tuberculosis requires surgery to relieve a cold abscess (aspiration) or obstruction due to pressure or adhesions from the nodes. The abdomen is closed without drainage in all types and the general treatment for tuberculosis is instituted. This includes streptomycin and also aureomycin.

Tuberculosis of the Anus and Rectum

Only about 3 per cent of the cases of fistula in ano are said to be due to tuberculosis. The diagnosis is made after examination of excised tissue. This is seen sometimes in infants, where general treatment is all

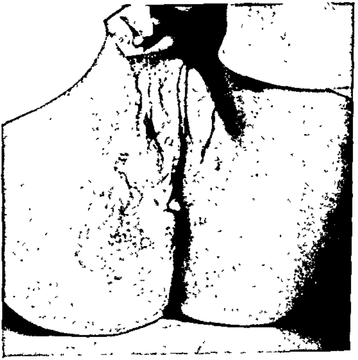

Fig. 75.—Tuberculosis of the perineum. Note the induration and multiple draining sinuses.

that is necessary. In adults, excision of the fistulous tract is required. Rectal tuberculosis is characterized by ulceration which causes pain, tenesmus, and even partial obstruction should a fibrotic structure result. A temporary colostomy may be necessary to divert the fecal current so that

healing may occur. Structures may be dilated or cut on the posterior wall of the rectum. Streptomycin may be used intramuscularly and locally as well. Sometimes resection of the rectum is necessary.

Tuberculosis of the Female Genital Tract

In women the reproductive organs are commonly affected by tuberculosis, although less commonly than the lungs, intestinal tract, and peritoneum. In almost every case of genital tract tuberculosis the Fallopian tubes are involved. The uterine endometrium is often affected—the ovaries in about one-third of the cases. The disease is always secondary although previously it was thought to ascend through the vagina and cervix—organs rarely involved. The primary focus is in the lungs, lymph nodes, or intestines. Tuberculosis peritonitis of the fibrocaseous type is a usual complication in adults. In children the lesions may be superficial and are accompanied by the ascitic or exudative type of tuberculous peritonitis. Such lesions may resolve spontaneously or after celiotomy. The symptoms vary with the type and degree of infection. In children there may be vague pains in the pelvis with indigestion, weight loss, fever, some distention, nausea, and vomiting. Appendicitis, mesenteric lymphadenitis, dermoid or other ovarian cysts, or anomalies may be simulated. In adults the disease resembles chronic pelvic infection produced by gonorrhea. There may be leucorrhea, pelvic pain, menstrual disturbances, sterility, or pelvic masses. Later the bladder and intestines may be involved producing signs of cystitis and intestinal obstruction. In all instances there may be evidence of tuberculosis elsewhere and the general picture of a chronic febrile malady. Since the diagnosis is often difficult, even with diagnostic curettage, exploration is indicated in the early stages. If the disease is not far advanced and is not the fibrocaseous variety, hysterectomy and bilateral salpingo-oophorectomy should be done. In children simple laparotomy may result in resolution. In the late stages surgery is apt to be useless, and it may be followed by multiple fecal fistulae and death. In all cases the general treatment of tuberculosis is indicated, including streptomycin.

Tuberculosis of the Genitourinary Tract

Tuberculosis frequently attacks the kidneys, ureter, bladder, and occasionally the epididymi, seminal vesicles, and testes. The disease is secondary to pulmonary tuberculosis or other foci in most cases. Ten per cent of all patients dying of tuberculosis have kidney involvement. Usually one kidney is involved. This phenomenon is said to be due to differences in resistance in the two organs. The renal cortex or pyramids are first affected; then the kidney pelvis, ureter, and bladder succumb. Almost any type of tuberculous manifestation may be seen—small tubercles throughout the kidney disseminated by the intertubular lymphatics (diffuse type), limitation to the pelvis (pyelitis type or pyonephrosis type), com-

plete destruction of the kidney, occlusion by the ureter with kidney atrophy (autonephrectomy)—or there may be calcification. The bladder is involved early, beginning often about the ureteral orifices.

The symptoms begin with frequency of urination. Later there is urgency, and finally incontinence. The urine is usually bloody which later becomes muddy due to lymphocytes, cellular debris, and bacteria.

The diagnosis is made by x-ray (retrograde pyelogram), the finding of tubercle bacilli in the urine, or the injection of the urine into a guinea pig with positive results. The treatment is general in character, with streptomycin later; nephrectomy may be done if the disease is advanced in one kidney. If the epididymis, seminal vesicles, and testicles are involved, *orchidectomy*, *epididymectomy*, and *seminovesiculectomy* are done.

Pleural Tuberculosis

Pleural tuberculosis is secondary to pulmonary infection in most instances; occasionally it results from tuberculous lymphadenitis of the mediastinal lymph nodes, and rarely it is said to be primary. The incidence of this form of tuberculosis has increased greatly since the employment of artificial pneumothorax. It is probably a complication in a mild or more severe form in 50 to 75 per cent of patients on whom this therapy is employed. Tubercle bacilli gain entrance to the pleural space from tubercles adjacent to the visceral pleura, bronchopleural fistulae, spontaneous rupture of pulmonary lesions (spontaneous pneumothorax), or tuberculous lymph nodes. Two clinical types are seen: pure tuberculosis and tuberculosis with pyogenic infection. The former causes the formation of variable amounts of straw-colored, more or less turbid fluid (pleural effusion); the latter is purulent and may be due to the tubercle bacillus alone (tuberculous empyema) or to an associated pyogenic infection (mixed tuberculous empyema). The diagnosis is established by clinical symptoms and signs, x-ray examination, and thoracentesis. It may be difficult to find the tubercle bacillus in the fluid, in which case guinea pig inoculation should be done. Treatment of the pleural effusion type depends upon its amount and the condition of the underlying lung. If very small in amount with moderate lung collapse and minimal involvement, it should be unmolested. Here it is said to be useful in causing immobilization to some extent of the affected side and it may be well tolerated if streptomycin is used. If more than a very small amount is present repeated aspiration with or without thoracoplasty, depending on pulmonary involvement, is the treatment of choice. Since it is impossible to detect the amount or degree of pulmonary disease without x-ray picture of the lung, this should be done immediately after aspiration of the fluid. Some phthisiologists suggest incomplete aspiration (to prevent adhesions between visceral and parietal pleural) and pneumothorax in lesser degrees of lung involvement. Tuberculous empyema may be treated by aspiration with irrigation using streptomycin or penicillin or both. This form of therapy is not apt to be successful and will fail in the mixed type where

open drainage must be done. If the pleura is not greatly thickened, thoracoplasty will obliterate the pleural space. If the pleura is thick and unyielding, then thoracoplasty with resection of the underlying pleura (visceral and parietal pleural decortication) is done in stages. (See Chapter 19.)

If the lung will not expand sufficiently after decortication to obliterate the cavity even with the aid of thoracoplasty, then the cavity is filled with muscle and skin flaps.

Tuberculous Laryngitis

Tuberculous laryngitis is a complication of pulmonary tuberculosis. It responds well to streptomycin.

Pulmonary Tuberculosis

The diagnosis of pulmonary tuberculosis is made by all factors considered as outlined earlier in the chapter. Recently many x-ray features have been reinterpreted. The childhood type may resemble almost any lesion, and calcification is seen in coccidioidal infections; also in histoplasmosis. Therefore the diagnosis cannot be made by x-ray picture alone.

Surgery is playing an increasingly important role in the treatment of pulmonary tuberculosis. As in all locations of the disease, the general treatment including streptomycin is paramount and all local measures must be looked upon as adjuvants.

All types of surgical treatment are designed to remove the principal focus of the disease (lobectomy or pneumonectomy), to put the part at rest (collapse, compression), or to effect drainage (closed or open). This same philosophy is the guiding principle in the treatment of tuberculosis anywhere. Since securing rest is necessary to the treatment of most surgical cases, it should be considered first. Immobilization and compression of the lung reduces the size of alveoli and bronchi, preventing aeration. Immobility invites chronic passive hyperemia and lymph flow is retarded. This diminishes the absorption of toxins, improving the patient's general resistance. There results also a proliferation of connective tissue which limits and demarcates affected areas often obliterating cavities and pericavity lesions. An exudative process is then converted into one that is proliferative or fibroid. Expectoration is facilitated with the lung at rest and compressed and relaxed, ridding the lung of secretions and accumulated exudates and preventing their reaccumulations.

As in other tissues the disease may be predominantly exudative, caseous, or ulcerative; proliferative, productive, or fibrous. Needless to say, any or all types may be present in the same lung. Healing is accomplished as in other tissues by fibrosis and calcification. Nature in her attempt at spontaneous healing resorts to methods which the surgeon seeks to emulate. In the exudative type with a small fuzzy apical lesion (by x-ray) resolution is common. Here nature may require an effusion to

help her immobilize the tissue and by low fever, malaise, and anorexia she forces the patient to bed. In the caseous varieties more strenuous efforts are required of natural defenses. Patients are sicker, having fever of greater magnitude, night sweats, and loss of weight with prostration. The cavity may be obliterated by immobilization and an attempt at collapse produced by approximation of ribs, elevation of the diaphragm, and pulling over of the mediastinum to the affected side. The fibrous type indicates a good reaction to a disseminated process and will heal if cavitation is not present.

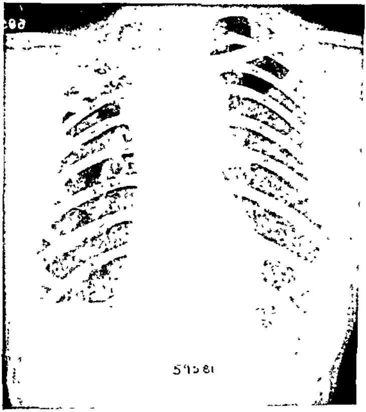

Fig. 76.—Healed tuberculosis of the lungs, adult type. The lesions are calcified.

Types of Surgical Therapy.—Indications for various types of procedures will differ with different clinicians, certainly in minimal and moderately advanced lesions, a sustained period of bed rest should be tried first. This may be supplemented by the use of streptomycin if healing is not prompt. If progress is not satisfactory, *collapse* therapy is indicated. If the lesions are far advanced, *compression* is used so that cavities may be obliterated. Collapse therapy is usually accomplished by *intrapleural artificial pneumothorax.*

Intrapleural Pneumothorax.—This is the most widely used form of treatment and is started by some phthisiologists after a trial of bed rest for thirty to sixty days. The cushion of air places the lung at rest and permits it to relax. However, it is usually started after bed rest for

four to six months and where hemoptysis is a prominent symptom and where the lesion is predominantly unilateral. It may be necessary to refill the pleural cavity with air for many years and it is always necessary to continue bed rest after pneumothorax has resulted in negative sputum. If adhesions exist between the visceral and parietal pleura, collapse may not be complete but should be tried. If results are not satisfactory these adhesions may be divided by intrapleural pneumolysis either as a closed operation (thoracoscope) or through an open thoracotomy (when adhesions are broad). Such adhesions are demonstrated by x-ray and fluoroscopic examination after pneumothorax and obviously pneumothorax must be continued after their division or the lung will become adherent to the chest wall again. Cavities may collapse whether adhesions are present or not. If they do not, other measures are used such as intrapleural pneumolysis, transpleural aspiration (Monaldi), external drainage (cavernostomy), or thoracoplasty (see cavitation). Partial pneumothorax may be used on both sides if vital capacity permits. Since tuberculous tissue collapses more readily than the normal, pneumothorax is said to be selective. It must be continued for two years or more to obtain the best results. Contraindications to its use are extensive bilateral involvement, asthma, advanced emphysema, and serious coexisting disease. Complications of the procedure are "pleural shock" (which is probably due to the administration of air, or traumatizing the lung) air embolism, serous effusion, tearing of adhesions, rupture of a superficial cavity, hemorrhagic effusion, secondary infection with empyema, tuberculous empyema, pleuropulmonary fistula, and tension pneumothorax as a result of tearing the lung.

Pneumothorax should be induced every two to three days at first; then as the air is less readily absorbed every week or two. With the needle in the seventh interspace the water manometer will fluctuate between −7 and −12. This shows a "free" rather than adherent pleural space. About 300 c.c. of air are given at the first sitting. This should reduce the manometer readings. With the aid of the fluoroscope and manometer, air is injected at intervals until complete collapse is obtained and the manometer shows little fluctuation, −1 to −3.

Extrapleural Pneumothorax.—This procedure has been used in cases of bilateral, apical disease of the lungs with cavities and also in patients who have dense adhesions between the visceral and parietal pleurae. The operation is not mutilating, can be done in one stage, and is a reversible procedure. *Technique*: Usually the fourth rib is resected after the periosteum is incised and then a cleavage plane is established between the parietal pleura and the endothoracic fascia. The lung is freed from the thoracic wall extrapleurally down to the sixth or seventh rib posteriorly, anteriorly to the fourth rib, and medially as far as the mediastinum. The space is filled with sterile saline solution and the incision is closed. Subsequently this space is filled with air in sufficient amounts to maintain a collapse.

Pneumoperitoneum.—Pneumoperitoneum is a procedure sometimes used in bilateral pulmonary tuberculosis, especially if basal. Air is injected under the diaphragm on both sides. It is used above or in conjunction with other forms of collapse therapy.

Intrapleural Pneumolysis.—Sometimes adhesions prevent collapse. These may be divided by the "closed" method with the aid of a thoracoscope (Jacobaeus, Coryllos) or the "open" method by incising the pleura and dividing the adhesions under direct vision after doubly ligating them. The dangers of the closed method are injury to the lung with resulting tension pneumothorax or bronchopleural fistula (therefore, adhesions are divided close to the chest wall), effusion and empyema, hemorrhage from lung tissue or directly from the great vessels, and injury to the pericardium. The open method is safer and permits ligation or cauterization of all vessels so that broad bands may be severed.

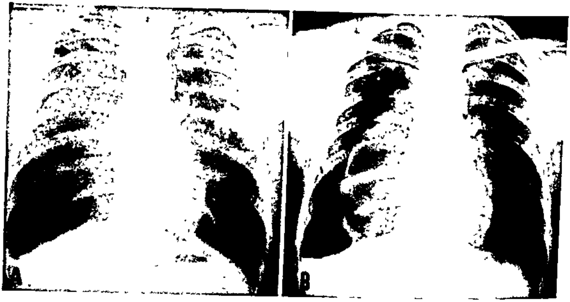

Fig. 77.—Cavitary tuberculosis treated by open pneumolysis (pneumonolysis); and pneumothorax. Patient, F. P. F., was a man aged 45 years. Cavitary tuberculosis of the right apex was present. The sputum was positive.

A. X-ray picture, arrow points to the cavity in the right apex and a dense adhesion between the visceral and parietal pleura Artificial pneumothorax was started, but this could not be effective because of the dense adhesions.

B. X-ray picture showing the effect of pneumolysis and artificial pneumothorax. There is good collapse four months after the operation. Sputum which was positive before surgery is negative now and was for fifteen consecutive daily sputum analyses. The operation was done under local anesthesia in the midaxillary line in the third interspace. Ribs were spread apart and the adhesions were divided and tied so that there would be no bleeding. By the open method it is possible to divide broader bands than it is by the closed method which may be done through the use of the thoracoscope. (Case referred by Dr. Russell Henry.)

Interruption of Phrenic Nerve.—This procedure produces a paralysis of the diaphragm, making it entirely passive. Usually it rises to a degree depending on intrathoracic pressure as influenced by adhesions or effusions and intra-abdominal pressure. Sometimes there is paradoxical movement (see chapter on empyema). It is said to reduce the volumetric capacity of the chest from one-sixth (400 c.c.) to one-third (800 c.c.) (Hegner).

The nerve may be crushed (phrenic emphraxis), cut (phrenic neurectomy), or avulsed (phrenic exeresis). Crushing the nerve produces a paralysis of the diaphragm for about six months. Accessory phrenics are occasionally encountered. They must also be crushed. Phrenic division produces a permanent paralysis. In avulsion the accessory nerve is usually removed with the main branch. Although usually a simple procedure, many complications may occur unless care is exercised. Hemorrhage, air embolism if one of the large veins or arteries are injured, tearing of the thoracic duct, and injury to other nerves (recurrent laryngeal, vagus, cervical plexus) in avulsion have been reported. If the nerve is avulsed, mediastinal hemorrhage or injury to the pericardium or lung may occur. Because of its dangers, phrenic avulsion is to be condemned and is no longer employed by most surgeons.

The indications vary with different observers. Some believe the procedure to be useless or to be actually contraindicated because the upper part of the lung may actually have to work more to compensate for the relative inactivity of the lower lobes. Others prefer it to pneumothorax. In general it may be looked upon as an adjunct to pneumothorax or thoracoplasty, particularly in lesions in the lower chest. However, the operation does stop the pumping action of the diaphragm and gives rest to the lung and it also decreases the size of the lung and allows it to relax, thereby facilitating healing.

Thoracoplasty.—Compression of the lung is best secured by the subperiosteal resection of ribs over the affected side. Should symptoms persist after pneumothorax and phrenicotomy, thoracoplasty may be used. Usually fever, cough, hemoptysis, and positive sputum result from persistence of a cavity. However, chronic fibrotic lesions without cavities or severe hemorrhage with cavities that do not readily collapse may not respond to pneumothorax and may require thoracoplasty. Fluoroscopic examination after the introduction of 200 to 300 c.c. of air will reveal the stability of the mediastinum (see Chapter 19). If fixed, mediastinal flutter will not occur after thoracic compression operation. However, a pneumatic jacket is put on to prevent parodoxical respiration.

Thoracoplasty has other indications than those mentioned; namely, chronic empyemas, tuberculous or pyogenic. It should not be used if there are recent lesions in the other lung or elsewhere in the body or in the presence of severe asthma, emphysema, or associated debilitating disease (diabetes, nephritis, heart disease). The operation is serious, requiring careful preparation of the patient. It should be done in stages. Often resection of the upper three ribs is sufficient. Usually three or more stages are required, two to three weeks apart, depending on the patient's reaction to the procedures. In this way the upper ten ribs may be removed. The first stage usually is the most difficult, for here the first, second, and usually the third ribs are removed. The third rib is removed first and then the superior ribs in sequence, leaving the first rib for attack after ample space has been secured by the removal of the lower ribs. The

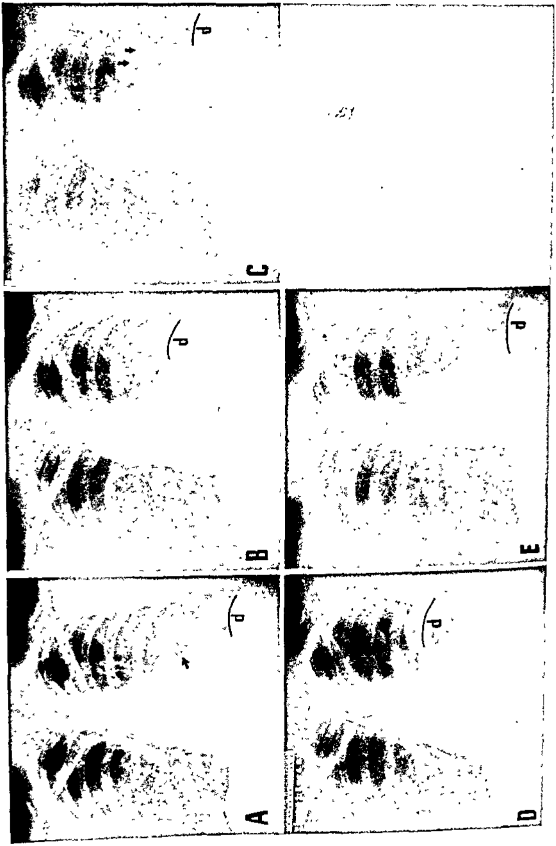
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Fig. 78.—Phrenic crush. *Basal tuberculosis* of the left lower lobe, treated by *phrenic crush* The patient, J. R., a woman 42 years old, had tuberculosis of the left base and a persistently positive sputum. Pneumothorax was unsuccessful in arresting the progress of the disease. The patient also had a tuberculous laryngitis. This was an ideal case to be treated by immobilization of the diaphragm. Accordingly, a phrenic crush was done. The diaphragm in its paralyzed condition rose to a high level, immobilizing lower lobe. This procedure was repeated on several occasions. The patient has remained well. The sputum has been negative.

The operation is done under local anesthesia through a small transverse incision above the clavicle and lateral to the lateral border of the sternocleidomastoid muscle The operation of phrenic crush is to be employed when the diaphragm is immobilized for short periods only. This, as the name implies, consists of crushing the nerve with a hemostat. Phrenicotomy is a division of the phrenic nerve and is to be used where a more permanent paralysis is desired. If regeneration is not to take place, a small piece of the phrenic nerve should be excised. This is known as phrenicectomy. The old operation of phrenico-exeresis is no longer employed because of its dangers and also because it is unnecessary.

A. November, 1945. Cavitary tuberculosis of left base. *B*. February, 1946. Diaphragm in paralyzed position. Cavities not discernible. *C*. January, 1948. Cavities open again Diaphragm in normal position. *D*. February, 1948. Phrenic crush—diaphragm high and immobile. *E*. July, 1949. Lung healed. Diaphragm resumes its normal function. (Referred by Dr. David Stone.)

transverse processes of the vertebrae are usually removed in order to prevent the collapsed lung and its cavity from falling into the paravertebral gutter, thereby escaping compression. Some surgeons remove the posterior portion of the ribs through small posterior incisions and the sternal portions through anterior incisions. Usually an adequate posterior incision with careful hemostasis permits a complete removal of the ribs. Local anesthesia, supplemented with intravenous Pentothal Sodium, may be used. Our preference is ether by endotracheal tube.

Thoracoplasty produces a collapse of the cavernous lung and results in an arrest of the disease in over 90 per cent of the patients. The mortality varies between 5 and 10 per cent, depending upon the type of risk which is selected. The procedure is, of course, irreversible and does produce some deformity. It is not useful in bilateral tuberculosis.

Fig. 79.—Thoracoplasty in the treatment of cavitary tuberculosis. A. K., a woman 38 years of age, with cavitary tuberculosis of the right upper lobe. Widespread adhesions between the visceral and parietal pleura made it impossible to use artifical pneumothorax. Conservative treatment was ineffective.

A. X-ray photograph showing cavity in right upper lobe. *B*. X-ray photograph showing the effect of a two-stage thoracoplasty in which the upper three ribs and transverse processes were removed in the first stage, and then two weeks later the fourth and fifth ribs were removed together with the transverse processes This is selective collapse and, in addition, it does not compress the hilus, thereby reducing vital capacity. Sputum analysis done recently is negative (Caso referred by Dr. Russell Henry.)

Chronic Cavities.—Chronic cavities which do not respond to the foregoing procedures may be obliterated by other methods. Sembs' *apicolysis* detaches the apex of the lung from its attachments, permitting the apex of the lung to collapse downward. This is done is addition to resection of the first three ribs. *Oleothorax* is the injection of oil instead of air to collapse a cavity. The oils employed are Gomenol, Iodipin, paraffin oil, and olive oil. Since oil is more slowly absorbed than air, its sustained effect is said to be of more value than pneumothorax. It is not widely used in this country. Like oils injected elsewhere (bronchi, spinal canal), it may be very irritating. It should be aspirated after this treatment is aban-

doned. Plombage or the injection of paraffin plombes into the pleural cavity belongs in this group.

Scaleniotomy or cutting of the scalene muscles is used in combination *with other operations such as phrenectomy. As has been pointed out,* the latter immobilizes the base of the lung, but throws more work on the apex. With excision or division of the scalene muscles which are accessory muscles of respiration, the apex, too, is immobilized.

Tension cavities, *in which air may enter but due to a valvular mechanism* from a kinked bronchus or mucosal flap it cannot leave, are benefited by aspiration and suction as in closed drainage of the pleura. Monaldi, Vineberg, and others introduce a needle and then a small tube through the intercostal space. *The pleural surfaces must be adherent. Gentle suction* is then applied.

Fig. 80.—Thoracoplasty. Seven-rib thoracoplasty in the treatment of left upper lobe cavitary tuberculosis. The patient, S. M., was a woman 32 years of age who had three cavities in the left upper lobe, the largest measuring approximately 3 cm. in diameter. The lowermost cavity was in the lower portion of the upper lobe close to the lingula. A two-stage thoracoplasty was done. The first three ribs, together with the transverse processes, were removed at the first stage, and the second stage included the fourth, fifth, sixth, and seventh ribs together with the transverse processes. A five-rib or a seven-rib thoracoplasty must be done so that the scapula will not ride inside and outside of the sixth rib when this is left in place

The effects of seven-rib thoracoplasty are demonstrated in the x-ray photograph. Note the *collapse not only of the left upper lobe, but also a compression of the left lower lobe* which has occurred due to the scoliosis, with the convexity toward the operated side together with a narrowing of the lower ribs. This is not as selective as is to be desired because the function of the entire lung has been practically eliminated. This patient was last seen in June, 1949. The sputum did not contain any tubercle bacilli at that time.

Open incision (*cavernostomy*) *and drainage as for a lung abscess* is used in cases where other methods fail to collapse the cavity. The procedure was formerly employed and then abandoned because of a persistent tuberculous bronchopleural fistula. The use of streptomycin and penicillin help prevent this. Its use is limited to the peripheral *cavity in which* lobectomy is contraindicated and may be looked upon as a supplementary procedure to thoracoplasty.

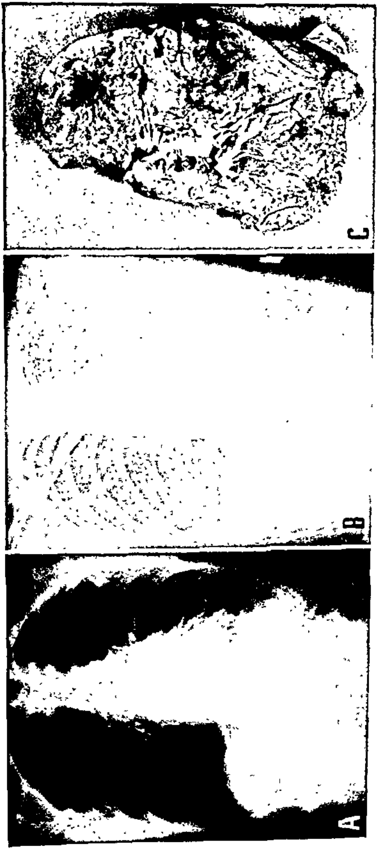
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Fig 81.—Lobectomy in tuberculosis. Lung resection in tuberculosis is indicated in the following conditions: (1) uncollapsed cavities following thoracoplasty, (2) tension cavities which failed to close under pneumothorax treatment as a result of bronchial disease; (3) cavities situated in the lower lobes which do not close under pneumothorax or with the aid of phrenic interruption or pneumoperitoneum; (4) bronchial stricture or bronchostenosis causing a shrinkage and bronchiectasis of the lobe; (5) tuberculoma; (6) disease which is stationary but which does not improve under conservative methods or less radical surgical methods. In other words, "a good chronic." By that term is meant a patient whose resistance to tuberculosis is high enough to prevent spread and yet not high enough to arrest the disease completely.

The dangers of lung resection in tuberculosis are many. There is usually a higher mortality, tuberculous empyema is a possible sequel, bronchopleural fistula is another, and spread to adjacent lobes or to other side is still another hazard. Streptomycin has lessened the latter considerably and is used routinely in the preoperative preparation of patients. The eradication of tuberculosis by resection is not to be considered as curative. It is a help in the arrestment of the disease but does not supplant medical management. These patients are all cared for over sufficiently long period of time to ensure a lack of spread. *C.* Photograph of the left lower lobe which possessed three of the indications listed: (1) There is a bronchostenosis, (2) there is a bronchiectasis, and (3) the disease is limited to the left lower lobe. Some tissue has been removed for biopsy. *A.* Bronchogram showing bronchiectasis of left lower lobe with narrowing of left lower lobe bronchus. *B.* Postoperative film taken five days after surgery. The patient, L. B., was a woman 30 years of age who had served with the Armed Forces in the Pacific theater. During this time she developed a cough which was persistent. On several occasions she had hemoptysis and lost weight. The sputum was positive and the x-ray examination demarcated the site of the disease as the left lower lobe. Bronchoscopic examination showed a bronchostenosis of the left lower lobe bronchus. Biopsy from some of the granulation tissue showed tuberculosis. Lipiodol was injected and bronchiectasis was present throughout the left lower lobe. The patient has had no further symptoms since surgery.

The indications for pneumonectomy in tuberculosis are more or less the same as those enumerated above. However, in general, when the disease has spread to a degree which involves the entire lung, the probabilities of arrestment are less than they would be if only one lobe were involved. Consequently, pneumonectomy, while offering much hope at first, has now not been practiced so generally. The entire question concerning extirpative procedures in the treatment of pulmonary tuberculosis rests upon the theory that the treatment is necessarily one of complete rest to the part involved as well as to the individual as a whole. In doing a lobectomy it is easily understood that the remaining lobes will undergo at least a compensatory emphysema to fill the space occupied by the removed lobe. Furthermore, it is conceivable that that remaining lobe would have to carry on a greater amount of work since per unit of space the number of alveoli have been decreased. The same holds true for pneumonectomy. The question naturally arises as to whether or not the added work induced by the removal of one lung or a part of a lung to the remaining lung tissue will act in an adverse manner so as to propagate the disease or invite a spread. To curtail the latter objection perhaps the use of thoracoplasty on the operated side, either selective in lobectomy or total in the case of pneumonectomy, may be helpful. Curtailment of expansion of remaining lung tissue would, of course, reduce vital capacity. There, again, the question arises as to how much crippling will be induced by extirpative surgery in addition to collapse therapy. (Referred by Dr. R. M. Vandivier.)

Lastly, in those cases of persistent cavitation, hemorrhage, or tuberculous tracheobronchitis which do not respond to streptomycin, pneumothorax, or phrenectomy, *lobectomy* or *pneumonectomy* may be indicated. (See Chapter 19.) These procedures carry a higher primary mortality in tuberculosis than the other operations which have been described and may be followed by serious sequelae such as spread to other lobes or the other lung, tuberculous empyema, or tuberculous bronchopleural fistula, or both. The use of streptomycin has reduced their incidence, making lobectomy relatively safe. Pneumonectomy is far more serious not only because it is a more extensive operation but what is more important, it indicates a more widespread dissemination of the disease. *In general extirpative operations are indicated in "good chronics"—patients who have lived with the disease for years without being cured in spite of various types of treatment and yet the disease has not spread to any great degree.* Indications are not clearly defined for lobectomy and pneumonectomy but at present we have employed them in (1) persistent tension (check valve) cavities with surrounding fibrosis; (2) tuberculoma; (3) tuberculous cavitation with bronchiectasis; (4) persistent unilateral or lobar tuberculosis of one side which has not spread to the opposite lung but which has not responded to less formidable procedures (permanent collapse procedures); (5) severe bronchial stenosis; (6) very large cavity; (7) hilar cavity; (8) lower lobe cavity; (9) progressive cavitary disease; (10) bilateral localized disease; (11) bronchopleural fistula.

Bone Tuberculosis

Bone tuberculosis is probably never primary. The original focus is in the lungs, lymph nodes, or gastrointestinal tract. The bones and joints are secondarily involved through the blood stream by involving capillaries already diseased by the tuberculous toxemia. Clumps of bacteria produce infarcts with tubercles as in other tissues. These are seen first in the metaphysis with subsequent involvement of the epiphysis and neighboring joints. Destruction of bone and joint results with deformity and cold abscess formation (see Chapter 21). Symptoms include swelling, muscle spasm which may be easily detected since the disease is usually monarticular, atrophy of surrounding soft tissue, usually out of all proportion to the disease of the part, pain, and deformity due to voluntary position, muscle spasm, or contracture. The diagnosis is made by a careful history, the general symptoms and signs of the disease with or without the discovery of the primary focus, x-ray examination, skin tests, and biopsy.

Tuberculous spondylitis (Pott's disease) causes a destruction of the vertebrae with subsequent collapse of the vertebral body and a resultant kyphosis. Frequently a cold abscess forms and follows the psoas muscle down to the femoral region (iliopsoas abscess) beneath the inguinal ligament. In the cervical region the abscess extends anteriorly and may burrow into the thorax. The treatment includes bed rest, with *immobiliza-*

tion by a frame or plaster cast, and the use of streptomycin. Spinal fusion *may be necessary*. In children, bed rest and sunshine may produce a cure.

Rollier of Leysen, Switzerland, believes that prolonged immobilization produces muscle and bone atrophy, thus decreasing local immunity. He prefers some motion, with rest in the sunshine on millet seed bags.

Fig. 82.—Advanced tuberculosis of the spine (Pott's disease), with kyphosis.

The hip, knee, ankle, shoulder, elbow, or wrist may be involved. Usually only one joint is affected. The part is immobilized to produce ankylosis in the most favorable position. (In children if treated early and persistently some degree of motion may be saved. Conservative measures are the rule with the aid of braces and casts. In adults operations are used to produce a bony ankylosis, arthrodesis.)

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Tuberculosis of Other Tissues

Tendon sheaths, the skin, and many other organs of the body are frequently involved. As was previously stated, no organ or tissue is immune.

Fig. 83.—Tuberculosis of the breast, showing conglomerate tubercle.

SUMMARY

The diagnosis of tuberculosis is relatively easy. The treatment may be summarized as: first, the general treatment of tuberculosis; secondly, local eradication, or arrest, by measures designed to localize the infection. It is readily seen that since there is no specific treatment of the disease, its successful management depends upon the care, rather than the cure, that the physician offers. Although streptomycin approaches a specific therapeutic agent in some types of the disease, it is the patient's resistance that produces a cure. The care of the tuberculous patient is based upon the theory that the disease will cure itself if the patient's general state of health is improved and the involved area is put at rest. Rest, then, to the body as a whole and to the affected part, and good food, fresh air, and sunshine, together with encouragement, constitute the chief methods of treatment. Streptomycin, para-aminosalicylic acid, and other antibiotics and chemotherapeutic agents constitute a formidable attack on the favorableness of the environment for bacterial growth and on bacterial proliferation. Many of the newer agents are still in the experimental stage. More will be forthcoming. The surgeon aids in securing arrest (1) by excising diseased tissue (lymph nodes, kidney (Fallopian tubes, lobes of lung, etc.); (2) by immobilizing bony parts through destruction or fixation of opposing surfaces (arthrodesis) or implantation of bone (Hibbs' or Albee's method

in two or three weeks. This constitutes the primary state of the disease and lasts until secondary symptoms appear six to twelve weeks later.

Secondary Stage.—The next stage may be looked upon as the dissemination of the germ and its toxins through the blood stream to all parts of the body. There is a syphilitic septicemia. Consequently, there are general symptoms and signs, such as fever, malaise, anemia, and

Fig. 84.—Chancre of the lip.

Fig. 85.—Chancre. Note the perilymphatic and perivascular round-cell infiltration.

general aching sensations. In addition, there are local manifestations. The first to appear is a *cutaneous rash* over the entire body. It may be macular, papular, pustular, or vesicular in type and involves even the palms and soles.

Mononuclear cells play the greatest part in secondary syphilis. If pustules form there may be many polymorphonuclears. Giant cells and fibroblasts are also seen.

Chapter 9
SYPHILIS

Syphilis is a contagious disease caused by the *Treponema pallidum (Spirochaeta pallida)* and transmitted by contact, usually venereal (acquired syphilis) or by inheritance from the mother (congenital syphilis).

The father infects the mother and she transmits the disease to the fetus. Some claim that the sperm may carry the treponema. However, the mother always has at least a latent syphilis and therefore the mother of a syphilitic infant shows an "immunity." The more recent the disease in the parent, the greater the chance for congenital syphilis in the offspring. The father with late tertiary syphilis, is not apt to infect mother or child.

The name *lues* means "plague" and is used often among physicians to conceal the identity of the disease in talking before patients. In Chapter 1 we learned that in 1530 Fracastorius wrote a poem about a shepherd, "Syphilis," who was afflicted with the "big pox" because he had blasphemed the Lord. Although the disease had been well known before and had been called the "big pox" to distinguish it from "small pox," the name of the fictitious, sacrilegious shepherd has clung to this affliction. It was not until 1905 when Schaudinn and Hoffman identified the small spiral, motile *Treponema pallidum* that the true cause of the disease was known. Then, in 1910, came the "curative" remedy of Ehrlich which we now know is only partially curative: salvarsan (arsphenamine and neoarsphenamine).

THE THREE STAGES OF ACQUIRED SYPHILIS

Primary Stage.—The acquired disease first manifests itself by an initial lesion known as the primary lesion, primary sore, or *chancre.* Usually this is seen on the genitals (glans penis prepuce, labia, vaginal wall, or, rarely, the cervix) about two weeks after exposure, but in some cases it occurs on the lips, and in accidental infection it may be seen on the hand or arm (the latter is seen occasionally in physicians and nurses). This is a painless ulcer which early involves the lymphatics, giving rise to enlarged, hard, painless, discrete inguinal nodes. In animals the organisms reach the regional lymph nodes within five minutes after entrance through the point of origin (Karsner). Since removal of the chancre does not necessarily stop the dissemination of the organism, some observers believe the primary lesion to be a lymphangitis with a local ulcer rather than an ulcer with a lymphangitis and lymphadenitis. The chancre is made up of small lymphocytes, fibroblasts, epithelioid cells, and giant cells (Langhans' type). The small arteries and veins show a thickened intima. This sore causes very little discomfort and disappears with-

Frequently the hair falls out (alopecia) and sometimes the nails are lost (onychia). A second and no less constant symptom is a sore throat. Small grayish *mucous patches* are seen not only in the throat but on the tongue and buccal mucous membrane as well. Condylomata lata occur on the cervix uteri. In addition, there are other lesions such as arthritis, retinitis, and even hepatitis. Frequently there is generalized, painless lymphadenopathy. The moist papules, open skin lesions, and mucous patches are loaded with spirochetes and therefore such patients must be in strict quarantine. Direct or indirect contact will spread the disease. The secondary stage may disappear within three or four weeks, or it may persist through relapse for a longer period. It is sometimes difficult to state when the secondary stage ends and the tertiary begins.

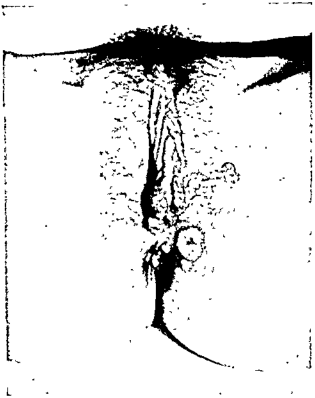

Fig. 87.—Syphilitic condylomata lata.

Tertiary Stage.—The third stage usually appears months or years after the initial lesion but may occur earlier. The lesions of this stage are the gumma (rare), diffuse fibrosis, and vascular changes. There may be tertiary lesions of the skin, mucous membranes, and cervix uteri which ulcerate and contain spirochetes. Gummas may occur in the skin, subcutaneous tissue, bones, muscles, liver, brain, lungs, kidneys, heart, and other organs. They are ulcerative lesions with overhanging edges and necrotic, caseous centers. The diffuse fibrosis or "hardening" which may

A. B.

Fig. 86.—Secondary syphilis. A. Macular skin lesions. B. Mucous patches on the tongue.

There is parenchymal atrophy. Such changes occur slowly over a period of years and imply the presence of the organisms for a long time. Calcification rarely occurs. The older the infection, the less contagious it becomes.

DIAGNOSIS

A history of exposure may or may not be obtained. However, the diagnosis is made by careful physical examination, by laboratory tests, and, if necessary, by therapeutic tests as well. Such routine examinations as eye tests (Argyll-Robertson pupil, inequality of pupils, muscle imbalance), knee jerks (absent in tabes dorsalis), and scars from previous lesions give an adequate lead to the diagnosis. If the patient is seen in the primary stage, a dark-field examination of the exudate from the sore will usually reveal the organism. The same is true of open secondary lesions, especially mucous patches in the mouth or around the genitals. Precipitation tests (such as the Mazzini, Kline, and Kahn tests) and the Wassermann complement fixation reaction aid greatly in the diagnosis. It should be remembered, however, that when negative they do not always rule out the disease and when positive they do not always attest to its activity. In addition to carrying out blood serological tests, the spinal fluid also should be examined for serological tests; the spinal fluid also should be examined for cells, globulin, colloidal gold curve, and Wassermann reaction. Last, if an internal lesion defies exact diagnosis, the therapeutic test is available: antisyphilitic treatment may be instituted and the suspicious lesions may disappear.

PROGNOSIS

The disease is a specific one with specific remedies. If the remedies are early and persistently applied, complete cure should be obtained.

IMMUNITY

There is perhaps some natural immunity to the disease. No doubt many who are exposed do not contract it. Also the disease is self-limited in a few. This is surmised by the occasional patient who has had the disease but who has had treatment. Yet after several years there is no clinical or serological evidence of it. Perhaps it still must be classed as latent. The disease itself may confer an immunity but for how long is unknown. If the disease is cured, then reinfection should be possible. Very few cases of this sort have been reported. Even though there is no clinical evidence of the disease the spirochetes may still be present.

The treatment begins with prevention. The press, governmental agencies, and an enlightened public have at last deemed it advisable to disseminate information concerning this scourge. If it is true that about 3½ per cent of the adult population has or has had the disease, it is well that this campaign is under way

occur in tertiary syphilis is the probable cause of syphilitic cirrhosis of the liver and paresis (hardening of the brain). These lesions, in turn, may be partially, if not altogether, due to the vascular changes that occur. The intima is thickened and forced inward by subendothelial swelling due to small mononuclear endarteritis, which interferes with the blood supply and results in a necrosis of tissue, or, if the process is extremely slow, in a fibrosis. Small round cells also extend widely around the vessels (perivascular round-cell infiltration). This stage may last throughout the entire life of the patient, which is usually shortened because of the disease.

Gummatous lesions may resemble tuberculosis, and as was pointed out in Chapter 8, the coagulation necrosis resembles infarction. The central portion of a gumma is firm, elastic, opaque, and yellowish-white. This is the necrotic, caseous part which does not tend to liquefy. The capsule is made up of dense tissue rich in epithelioid cells and mononuclear wandering cells. Giant cells are also seen. The whole arrangement is indefinite and irregular. This and the characteristic changes in the vessels help to distinguish the lesions. In the aorta, gummatous or diffuse syphilitic infiltration affects the adventitia and media, obliterates and destroys the vasa vasorum, and brings about hyperplastic changes in the intima. Perhaps in syphilis as in other infections, the type of lesion depends on the rapidity of its development since it is essentially vascular. A sudden occlusion might cause necrosis and sloughing, the more gradual may give rise to gumma, and the extremely slow may engender a diffuse fibrosis.

Although the pathological course of syphilis is subdivided as indicated, the biological course is divided into *acute* (first two years) *early latent* (third and fourth years), and the *late latent* (which may last the rest of the patient's life).

The reactions of tissues to syphilitic lesions follow a different course from that seen in nonspecific infections or in tuberculosis.

1. *Resolution* occurs frequently as in the chancre and secondary lesions.

2. *Necrosis and absorption* occur commonly because of a decreased blood supply and an improvement under treatment. The gumma is an example.

3. *Necrosis and sloughing* are seen in untreated cases, especially in bone and cartilage, but also in the skin and elsewhere; for example, saddle nose, sloughing of hard palate, sloughing of large areas of skin, etc.

4. *Suppuration* does not occur, nor does liquefaction take place as in tuberculosis. Occasionally a syphilitic lesion is secondarily infected, with resultant pus formation.

Healing occurs by cicatrization such as follows the destruction of tissue from any cause. There is, however, a "master process" which is frequently an end result regardless of the extent of tissue destruction. This at times is all that may be seen in an organ except for the infiltration of lymphocytes and plasma cells near the blood vessels and lymphatics.

lesion may occur as it does in other organs. Usually, however, the cause of such a process is diffuse scirrhous carcinoma. Other lesions resembling syphilis in the stomach are carcinoma, sarcoma (reticulum-cell and lymphosarcoma), Hodgkin's disease, fungus infections (actinomycosis, blastomycosis), tuberculosis, and anthrax. The diagnosis is suspected because a lesion of this size could be caused by only one other disease, malignant

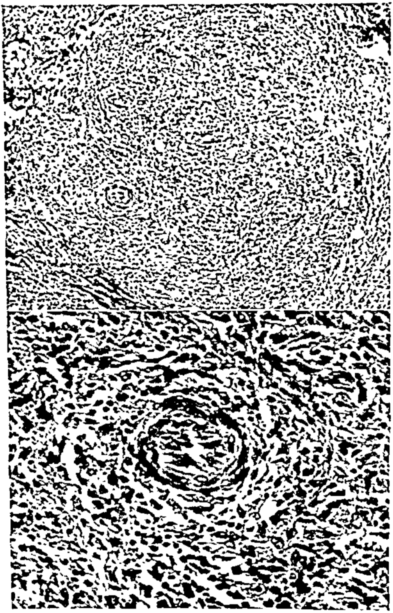

Fig. 88.—Photomicrographs of syphilis in the skin. *A.* (Low power.) Perivascular infiltration. *Note the nodular appearance of the lesion*; also the extent of the perivascular response which is not limited to the immediate circumference of the vessel but extends over a wide area This is important in the concept of this disease (as well as of others). The endothelium is first involved, then its surrounding tissue. *B.* (High power.) Thickened vessel Many lymphocytes, epithelioid, and mononuclear wandering cells are seen. The intima is thickened, as is also the adventitia. The media is partially destroyed.

In the past there were three types of treatment: the arsenicals (neoarsphenamine), the heavy metals (bismuth and mercury), and the iodides. These were employed usually in the order mentioned and were repeated until a cure was permanent. This required two, or even three, years of continued treatment but in most cases resulted in a cure or at least an arrest of the disease. Since the advent of antibiotics, such as penicillin, new strides have been made in the treatment of the disease. It may completely revolutionize the treatment of syphilis. Bacitracin may also help in the treatment.

SYPHILITIC LESIONS IN DIFFERENT TISSUES

Skin Syphilis.—In the primary stage the characteristic lesion is the chancre. In the secondary stage the disease manifests itself by the skin rash, mucous patches, and condylomas (soft warts about the genitals). In the tertiary stage large serpiginous ulcers may develop on the scalp, the chin, and the upper outer side of the leg. Any chronic ulcer of the skin should be studied for this possibility.

Syphilis of the Mouth, Nose, and Throat.—Syphilis of the mouth, nose, and throat is highly contagious. It is characterized in the secondary stage by mucous patches, on the tongue and buccal mucous membrane, and in the tertiary stage by gummatous ulcers of the tongue and floor of the mouth. The tongue ulcers are very often associated with carcinoma. Ulcers on the roof of the mouth (hard palate) frequently penetrate through into the nose, forming a dirty, secondarily infected opening, which permits regurgitation of fluids into the nose. The typical "saddle" nose may be a part of this same process or the result of a necrosis of the septum alone. Congenital syphilis may give rise to a chronic atrophic rhinitis. The discharge is foul—syphilitic ozena. *Diagnosis* is made by serological tests and, more important, repeated biopsies, then the therapeutic test. If healing is not progressing satisfactorily in two to three weeks, excision of the ulcer, especially of the tongue, is indicated for further study.

Syphilis of the Esophagus, Stomach, Intestines and Rectum.—If a patient has stomach or intestinal symptoms and a 4 plus Wassermann, this does not necessarily mean that the symptoms are due to syphilis. However, gastrointestinal lesions do occur in syphilis and may be revealed by gastrointestinal x-ray after barium meal. Syphilitic gummas of the esophagus usually resemble carcinoma. Biopsy should be done. The ulcers heal, leaving a stenosis. This is treated by careful dilation bougies. In the stomach there may be a large, deforming lesion of the fundus or pyloric antrum. Gummas may be single or multiple and are usually found in the submucosa. Gummas may ulcerate and then heal with scars which deform the stomach (hourglass contracture, plyoric stenosis). Formerly a diffuse fibrosis resembling linitis plastica was ascribed to the action of the *Treponema pallidum*. Undoubtedly such a

neoplasia (carcinoma or lymphosarcoma). If it were due to the latter, operation would be useless; therefore, a therapeutic test is tried and its effects observed by frequent x-ray examinations. If no improvement results, surgery is indicated. This may be necessary to relieve obstructions resulting from scar formation. Here gastroenterostomy, gastrogastrostomy, or pyloroplasty may be done. In large ulcerating lesions subtotal gastric resection is done. Rarely total gastrectomy may be necessary to excise all of the diseased tissue. In such instances, the surgeon usually feels warranted in doing the operation because (a) there is no healthy stomach suitable for anastomosis or (b) the possibility of carcinoma has not been completely ruled out.

Syphilis attacks the intestines in the congenital and acquired forms. The *small intestine* may be ulcerated especially in the ileum in the former but rarely in the latter form. Acquired syphilis may affect the colon, especially the sigmoid, the rectum, and the anus. As elsewhere, gummas may form with resulting fibrosis and stricture. In the small intestine or colon the constricted area may produce an obstruction requiring a short-circuiting operation or resection. In the rectum or anus such areas may require excision, but often simply dilatation with antibiotic treatment is sufficient.

Syphilis of the Liver, Spleen, and Kidney.—In the "parenchymatous" organs a diffuse fibrosis is often observed. Acute hepatitis, splenitis, and nephritis are seen in secondary syphilis and fibrosis in tertiary syphilis. The lesions produced are cirrhosis of the liver, chronic syphilitic splenitis, and nephritis.

As in other locations, gummas may occur even in congenital syphilis. Splenectomy is advocated by some in persistent syphilitic splenomegaly which resists antisyphilitic treatment when it gives rise to symptoms for mechanical reasons. It is also done in syphilitic cirrhosis of the liver in an effort to reduce the load of blood to the liver, thereby lessening its burden. Splenectomy in syphilis is of little value regardless of the indication.

Syphilis of the Bones, Joints, Bursae, Muscles, and Tendons.—Many medical historians believe syphilis originated in America and was carried back to Spain by the sailors with Columbus. However, there is no doubt that in Biblical times (about 3000 B.C.) the high priests knew and described an affliction with aching bones and joints and a rash. Secondary *syphilis causes a periostitis, a synovitis, and even a transitory arthritis.* In the tertiary stage we may find gummas of bone with irregular areas of destruction. Since syphilitic bone disease is an osteolytic and osteoplastic process, such areas may resemble osteomyelitis (nonspecific) with the formation of sequestra. These may require sequestrectomy. There may also occur osteitis but more often periostitis (saber tibia). The latter is due to an increase in cortical bone limited to the diaphysis on the convex side. The flat bones of the skull may show destruction with se-

Fig. 89.—Syphilitic leucoplakia of the tongue.

Fig. 90.—Syphilis. There is destruction of the nasal cartilages and the hard palate.

due to vascular lesions with resulting degeneration in the tertiary stage. Pathologically there may occur gummatous meningitis, syphilitic arteritis, myelitis, paresis, and tabes dorsalis. There are combinations such as meningoencephalitis, encephalomalacia, or myelomalacia as a result of syphilitic arteritis; meningomyelitis associated with syphilitic myelitis; myelitis together with paresis; and meningitis with tabes. Clinically, the gumma may produce symptoms like a brain tumor (see Chapter 18), which indeed it is. In congenital syphilis the meninges or nervous tissue may have gummas, or due to the surrounding inflammation, the meninges or brain may show edema, meningitis, encephalitis, or myelitis—these too may resemble a brain tumor clinically. Syphilis may cause a neuroretinitis or an atrophy of the optic nerve (primary optic atrophy), producing blindness; it may also cause blindness through *increased intracranial pressure and a choked disc (secondary optic* atrophy). Any of the cranial nerves or groups of nerves may be involved. A panophthalmitis may be due to a diffuse gummatous involvement around the cavernous sinus involving the third, fourth, and fifth cranial nerves (see Chapter 18). *Paresis* causes a "shrinking" in size and weight of the brain as a rule. The white matter may be soft and edematous. The gray matter is hard and there is considerable thinning with much neuroglia proliferation. Cells and tracts degenerate, producing mental changes clinically with "delusions of grandeur." Syphilitic arteritis of the brain begins in the adventitia with miliary gumma formaton or fibrosis. The media (atrophy of muscle) and intima *(thickening) are involved. A "stroke" of paralysis in a young man* (rupture of lenticulostriate artery) is often due to syphilis. *Cerebrospinal syphilis* gives mixed types of paralysis, and tabes dorsalis (locomotor ataxia) affects the dorsal nerve ganglia and posterior horn cells which are degenerated with destruction of the cells and axis cylinders. There is fibrosis in the posterior root ganglia but the cells are not destroyed. The lesion usually begins in the lumbar region, destroying deep muscle sense and producing the typical stamping gait. Often the urinary bladder is involved through its nervous innervation: this is known as *tabetic bladder,* a type of paralysis due to diminished sensation and producing painful urinary symptoms. Surgery is not often indicated in syphilis of the central nervous system. Rarely a subtemporal decompression may be indicated to relieve the increased intracranial pressure, thereby saving the eyesight while antispirochetal therapy is being used. The malaria treatment of paresis in addition to antisyphilitic treatment with penicillin has yielded excellent results. Since malaria and syphilis are protozoan infections it is thought that similar cellular and humoral reactions *are excited. It is a chronic or subacute infection* with an insidious onset; therefore any infection of this type which could be controlled would theoretically be useful in the treatment of paresis (see Chapter 4). The fever itself may help, but it is the number of episodes

questration (craniotabes) and the nasal bones may become necrotic, resulting in performation of the nasal septum. As a result of congenital syphilis children may show a bilateral synovitis (Clutton's joints) or metaphyseal areas of destruction associated with formation of new bone along the shaft; and in tabes dorsalis there may be a *painless* extensive destruction of the knee (Charcot's joints).

Syphilitic bursitis occurs in the tertiary stage. If chronic draining sinuses result with destruction of the bursa, medical treatment may fail; the bursa should be excised under such conditions. Myositis occurs in the secondary stage but it is usually transitory. Occasionally contractures occur. In tertiary syphilis a diffuse interstitial sclerosing process may be found, or there may be gummatous formation with ulceration and fibrosis after healing. Rarely surgery is necessary to relieve contractures.

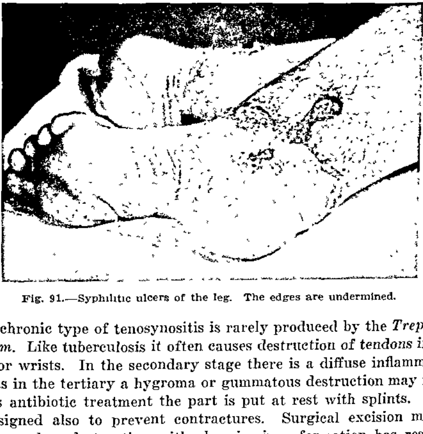

Fig. 91.—Syphilitic ulcers of the leg. The edges are undermined.

A chronic type of tenosynositis is rarely produced by the *Treponema pallidum*. Like tuberculosis it often causes destruction of tendons in both hands or wrists. In the secondary stage there is a diffuse inflammation, whereas in the tertiary a hygroma or gummatous destruction may result. Besides antibiotic treatment the part is put at rest with splints. These are designed also to prevent contractures. Surgical excision may be necessary when destruction with chronic sinus formation has resulted.

Central Nervous System Syphilis.—Some syphilologists believe that a special strain of spirochete is responsible for syphilis of the brain and spinal cord (neurotropic strain). This may be true, but anyone who is afflicted with the disease may have the infection spread to the central nervous system. The syphilitic lesions are the same as in other parts of the body and produce their effects through inflammations of the meninges, glial overgrowths, gummas, fibrosis, and diminished blood supply

fected the wet-nurse. Secondary lesions of the skin and nipple occur *commonly. Gumma of the breast is rare in tertiary syphilis. Surgery* is rarely indicated.

Syphilis in Other Organs.—No tissue or organ is immune. The *testis* is affected in acquired syphilis before the epidymis—this is the reverse of the sequence in tuberculosis. As in other organs, the two lesions that may occur are gumma and diffuse fibrosis. In either there may be sexual impotence. However, this is more often not the case even

Fig. 92.—Congenital syphilis, showing saber tibia.

in the presence of an active lesion. The *treponema pallidum* thus has easy access to the sperm The *pancreas* may be affected in congenital syphilis Here a chronic interstitial pancreatitis with increase of connective tissue results. A diffuse fibrosis occurs in the acquired variety. Pancreatic function may be reduced.

The *thymus* is more often involved in congenital syphilis. Such infants may have the so called Dubois abscesses which are cystlike cavities probably due to softened gummas. The enlarged thymus may produce transient respiratory distress.

of chills and fever and the time element which seem more important than the degree of fever. Artificial heat therapy is not so effective and unless carefully controlled may be harmful to brain cells. Tertian malaria (Plasmodium vivax) is usually induced because it is mildest and most easily controlled. *Other fevers are produced by the injection of typhoid* vaccine, sulfur preparations and non-specific proteins (milk, horse serum).

Syphilis of the Circulatory System.—The heart and blood vessels are always somewhat involved. Syphilitic heart disease (myocarditis, endocarditis, and pericarditis) and aneurysm (chiefly of the aorta but even of other vessels) are not uncommon. Gumma formation does occur in the arteries. More common lesions are syphilitic mesaortitis. The aorta is affected due to an endarteritis of the vasa vasorum which first involves the adventitia, then the media, and, finally, after cicatrization, the intima. The muscular and elastic coats are destroyed and replaced by fibrous tissue which stretches, dilates, and predisposes to aneurysm. In accessible vessels the aneurysm may be obliterated surgically (see Chapter 17). Syphilitic inflammation of the smaller vessels also occurs. This is exemplified in syphilitic arteritis of the brain as previously described. The veins may show periphlebitis, phlebitis, and thrombosis.

Syphilis in Bronchi and Lungs.—Syphilis involves the larynx, trachea, and bronchi in much the same fashion. During the secondary stage transient superficial papules and ulcers occur. The tertiary stage brings gummas which are usually small and flat, often nodular, producing obstruction. The vocal cords may be destroyed by ulceration or rendered functionless by secondary cicatrization. The lungs are more often involved in congenital syphilis. Here there may be one or many gummas in association with pneumonia alba. In acquired syphilis a single large gumma is the most characteristic lesion. It is rare and is usually located in the middle or lower lobe. Fibrosis may extend around the lesion or may be a separate diffuse process. The importance of the lesion is that it resembles tuberculosis or neoplasm clinically and even roentgenologically. Surgery is rarely indicated. But if a large gumma fails to heal under medical treatment, lobectomy may be indicated. This is especially true because of the danger of overlooking carcinoma.

Syphilis of the Uterus, Fallopian Tubes, and Breast.—The cervix is not often affected by the spirochete although, as has been mentioned, chancre (primary stage) condylomas (secondary), and gumma (tertiary) do occur. The uterus is rarely affected; the Fallopian tubes almost never, but there may be gummatous lesions. The breast is also rarely affected. Chancre of the nipple is seen and has been observed bilaterally. Sexual perversion may be a cause of this but more commonly the condition was seen during the era of wet-nursing, when a syphilitic infant often in-

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Congenital Syphilis.—". . . visiting the iniquity of the fathers upon the children unto the third and fourth *generation* . . ." (Exodus 20:5) may have referred to congenital syphilis. However, as a matter of fact, it fortunately is not carried to the third generation. It is hoped that the new "hygiene laws" and attempts at eugenics will diminish the incidence of this affliction. Congenital syphilis is not hereditary. It is acquired in utero. Spirochetes are in the placenta. They are also found in semen and some syphilologists believe they may be carried by spermatozoa and may enter the ovum at the time of conception. This is unlikely for the ovum so fertilized would probably not develop or if it did abortion would follow. The syphilitic newborn frequently presents an ugly picture with snuffles (rhinitis), rhagades (fissures about the mouth), mucous patches, and general emaciation, making the "old man" appearance. Routine Wassermann tests of mothers and babies are now done so that treatment may be started early. Treatment of the syphilitic pregnant mother may prevent the transmission of the disease to the fetus. Should the child survive, he may develop one or all of Hutchinson's triad: notched or pegged upper incisor teeth (permanent teeth), eighth nerve deafness, and interstitial keratitis. In addition there may be deformities of the head (prominent parietal bosses), Pitting of the molars, saddle nose, saber tibia, etc. In spite of treatment these stigmas may leave their marks for life.

Summary

Syphilis is a protean disease, mimicking almost every other ailment known. The diagnosis is not always easy. The possibility of this infection must always be considered in any diagnostic problem. The surgeon is sometimes called upon to perform an operation to remove necrotic tissue from bone, to relieve intracranial pressure, to obliterate aneurysms, to correct deformities by plastic surgery, and to release obstructions. Occasionally organs may be so hopelessly destroyed as to demand removal (spleen, testicle). Although necessary surgery is never contraindicated because of the presence of syphilis (except in cases of acute secondary syphilis), medical treatment should always be used to complete the cure. Syphilis per se does not retard repair; however, the poor general health of a syphilitic person may do so.

Syphilis of the tongue may initiate carcinoma. Syphilitic strictures of the rectum and bowel, gummas of the brain, and syphilitic obstruction of the stomach may demand surgical aid.

The prevention of this horrible malady is entirely feasible. A clean, continent life is possible to youth if adequate instruction is given. Wide publicity at present is bringing the entire problem before the adult population. This should be supplemented by correct education, given by the physician himself. Strict quarantine of those afflicted until they are cured will complete the abolition or bring to a minimum the incidence of syphilis.

bears, their constitutional type, their age at death, and the probabilities of one's own future, and even though he be uninterested himself, certainly medicine may know more about the life history of disease.

Due to the complex nature of hereditary factors a pure constitutional type is rare. The average person is a mixture of types. However, in spite of these blends there are three big groups; namely, (1) the linear, slender, asthenic, introvert, hyperevolute, susceptible, leptosome, longitudinal, dolichomorphic; (2) the lateral, broad, hypersthenic, extrovert, hypoevolute, nonsusceptible, pyknic lateral, brachymorphic, plethoric, apopleptic, gouty, round; (3) the intermediate type having some characteristics of each.

Shakespeare knew the two types when he wrote, "Tragedie of Julius Caesar." In Act I, Scene II, Caesar says:

"Let me have men about me that are fat;
Sleek-headed men, and such as sleep o'nights:
Yond Cassius has a lean and hungry look;
He thinks too much: such men are dangerous."

The weave and texture of the cloth of a coat determines its ability to withstand wear and tear, its suitability for fashioning into a garment, its ability to protect its wearer. It is this texture and weave that we wish to examine in defining man's constitution as well as his outward appearance.

INFECTION AND THE HUMAN CONSTITUTION

According to Draper there are four general forces which cause disease. Unless these forces are extreme in their action, they are successfully overcome by the four panels which nature has built into man's constitutional make-up. *Overwork* is combated by the *anatomical* panel; *overeating*, by the *physiological* panel; *overworry*, by the *psychological* panel; and *germs*, by the *immunological* panel. Let us see what is meant by the immunologic panel in man's constitution, and how it combats infection.

It is rare to find a man with four panels equally strong and this difference makes for individual, constitutional types. The mere presence of the meningococcus in the environment does not constitute the disease meningitis. There must first be a conflict—then there is a difference in the reaction of the individual to the meningococcus—A gets the disease and B does not. There has been much work on the meningococcus but not enough on why A is susceptible and B is not; or why two children with the same parents and the same environment differ so markedly in their resistance to disease That is, there may be the same *idiotypic influence* (heredity) and the same *heterotypic influence* (environment), yet the *phenotypes* (the resultant of both influences) are not the same, in so far as their immunologic panel is concerned. To use the vernacular, one child "gets everything that comes along, but the other is as tough as leather." How

PART III

GENERAL REACTIONS TO INJURY

Chapter 10

THE HUMAN CONSTITUTION

In previous chapters we have observed the body's reactions to mechanical injury and bacterial trauma and its behavior in miscellaneous infections, tuberculosis, and syphilis. In this chapter we shall try to account for differences in reactions to injury and disease and for the probable endogenous factors which may be responsible for certain ailments. In so doing we should begin with a consideration of the human constitution, including its hereditary and environmental origin. This should enable us to understand in a better way the source of compensatory mechanisms which come into play in response to injuries of all kinds, including those of unknown origin (neoplasia), as well as to those abnormal states brought about by disturbances in acid-base balance and water balance and those due to hemorrhage and shock. These subjects are discussed in following chapters. However, it should be mentioned here that these compensatory mechanisms are constantly at work. They are ample to care for ordinary physiological, immunologic, or psychological abnormalities and they usually respond without discernible symptoms and signs. It is only when ordinary reactions fail to restore normalcy that nature resorts to more drastic reactions in an effort to save life. Here certain syndromes are noted such as shock, acidosis, alkalosis, dehydration, etc.

In fact, it is the strength of compensatory mechanisms which prevent what we ordinarily call sickness. In a broad sense the clinical symptoms and signs of sickness are due to the fact that ordinary "reserves" are unable to cope with an injury, whether it be bacterial, chemical, thermal, or other kinds. If these resistance factors were strong, nature would not resort to extreme prostration or high fever, etc., to meet the issue. Sickness, then, in a clinical sense is a group of symptoms and signs which are a part of these compensatory mechanisms stimulated to a degree which makes them evident.

Some believe that a discussion of the human constitution is abstruse, indefinable, and academic. Others aver that classification of constitutional types and their heredity may lead to a more accurate understanding of disease, its origin, and prevention. Indeed by going to the health department file one may look up the cause of death of his fore-

serious illness, such as empyema, typhoid, spreading peritonitis, etc. Within a few years they are obese and remain so. Racial resistance to certain organisms is peculiar to definite constitutions: certain reactions to disease may be inherited through generations as actual constitutional qualities. This tendency is seen in allergic states. The formation of polypoid hyperplasia in the paranasal sinuses is directly attributable to protein sensitization. The infection that usually supervenes is entirely secondary and is probably caused by an interference with proper drainage. Many examples of racial immunity are known, such as the apparent freedom of the Negro from yellow fever, as opposed to his susceptibility to tuberculosis.

In evaluating this state called immunity, we are struck with the maze of conflicting evidence as to how immunity occurs. Immunity to certain virus diseases is said by some to be due to maturation of the individual; by others, to the individual's having contracted the disease in a subclinical form upon his initial exposure to it. Immunity to any disease may be natural or acquired, relative or absolute, local, general, or both local and general. Absolute immunity is uncommon in man. On the other hand, man usually has some immunity to all diseases, with the possible exception of glanders. In lower animals there seems to be an absolute immunity to leprosy.

There is increasing evidence of the transmissibility to man of diseases peculiar to lower animals (for example, undulant fever, tularemia, rabies, etc.). The reverse seems to be true also.

Our immunity is necessarily relative and depends upon the virulence, number, and kind of bacteria as against the state of health, local resistance, and constitutional type of the individual.

Some investigators now believe that every tissue in the body has cells which may become phagocytic under proper stimulation. When dyestuffs such as trypan blue are injected into animals, granules appear in macrophage cells everywhere. In rats the skin and mucous membranes remained blue for three months. Niemann made an incision in such animals and sewed a small gauze sponge under the skin. Nine days later the dye had colored the sponge, and the skin and mucus membranes began to lose their color. This means that the reticulo endothelial cells were transported to the site of the infection (see Chapters 4 and 5). The "blocking" of the reticulo-endothelial system was thus cleared, and its functional activity was increased. Infections which terminate favorably may in this way stimulate the functional activity of the reticulo-endothelial system. Menken showed that trypan blue, when injected intravenously, accumulates in the tissue of an inflamed area. The same is true of bacteria. This suggests that the well known tendency of infection to occur in a place of lowered resistance is due to an increased permeability of the capillaries (see Chapters 4 and 5). Perhaps, too, this explains the phenomenon of Arthus and Shwartzman (that is, when a bacterial toxin is injected into the animal intravenously, there occur violent local inflammation and sloughing).

The normal individual is one who meets and conquers the ordinary adverse forces in nature. Immunity seems to be due to cellular phago-

can we tell the A type from the B type—the asthenic, linear, introverted, hyperevolute and susceptible type from the pyknic, lateral, extroverted, hypoevolute and nonsusceptible type? Morphological, physiological, and psychological studies will help us. Moreover certain immunologic tests help to determine types. Examples of such tests are skin reactions to protein, metabolism tests, the Dick test for susceptibility to scarlet fever, the von Pirquet and Mantoux tests for tuberculosis, the Schick test for susceptibility to diphtheria, etc. The susceptibility of a child of the linear type to infections such as tuberculosis, rheumatic fever, and diphtheria is pointed out by Hurst and others and is a common observation.

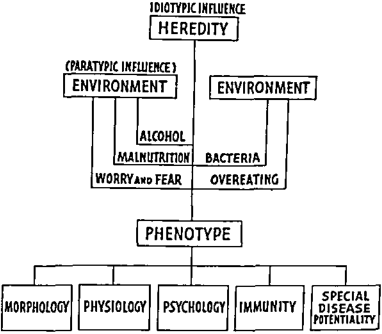

Fig. 93.—Diagram illustrating Draper's theory of phenotype. The idiotypic influence (heredity) is perhaps stronger than the paratypic (environment). Both produce the completed product (phenotype), whose constitution is divided into four panels and a special disease potentiality. (Redrawn from Draper.)

What is immunity? The dictionary defines it as "a state, natural or acquired, in which the body is resistant to disease." Stockard has said, "The same disease-causing organism does not produce the same effect on all personalities. These differences are not all due to differences in the constitutional quality of the individual persons attacked." *Immunity may be said to represent the changes in the constitutional state produced by germs.* These changes (called *immunity*), or the processes by which they are acquired, may in themselves set up constitutional states which modify or deviate to some extent the further growth and developmental qualities of the individual. The immunologic panel is therefore a varying part of each individual type of constitution—but, because of its modifying influence, it may be the *cause* of a particular constitutional type. We have all observed children of the so-called linear type recover from a

door." And conversely, the mere presence of an inflamed area does not constitute an infection or a general septicemia. Draining an abscess does not cure an infection; it aids the forces of immunity (which caused the infection to localize). We are apt to say that our particular type of antiseptic, antibiotic, or chemotherapeutic agent or method of treatment *cures* and to forget the patient in the equation. We have shown that granulations in a surgical wound after the sixth day are immune to staphylococci rubbed on them, and this observation, no doubt, applies to man as well as animals.

Infection and resistance may truly be compared to a fight. It is not guerrilla warfare with a haphazard defense by ill-trained and inexperienced troops. It is, in those individuals with a high degree of immunity, a well-organized and systematic defense, the details of which we may clearly observe in the superficial abscess.

It is the degree of organization and ability of the soldiers of the reticulo-endothelial system to fight that determines whether a given pnenotype which heredity and environment may produce has a strong or weak immunologic panel. Even the streptococcus, which fights from ambush as a sniper, does not take the strong constitutional type by surprise. His warriors have come down to him from his ancestors, well fitted to cope with these enemies. This, indeed, has made it possible for man to survive. Potential enemies of this sort exist in many tissues of the body at all times. There are probably small areas of infection and inflammation continually present in various parts of the body. These areas have been called chronic, symptomless, silent foci of infection. In view of present concepts, we may conclude that the individual with a good immunologic panel is well able to cope with such areas of germ life. His forces of resistance are acquainted with these indigenous bacteria and, if not interfered with, will destroy them completely, wall them in, or keep them harmless. To try to eradicate all of them would obviously be impossible, and, in the light of present knowledge, entirely unnecessary.

Applying our discussion in a practical manner, we may say that the *constitutionally strong survive the ever-present bacteria, and that in those not so strong it is far easier to build up the immunologic panel than to attempt the eradication of every potential area of infection of endogenous or exogenous source.* Every other panel is directly associated with the immunological. Anatomical (strong physical bodies), physiological (proper food), psychological (happy, wholesome outlook, psychosomatic factors)—each, in turn, helps the other. Since the advent of chemotherapy and antibiotics we are more than ever aware that *an infection is* overcome by body resistance. The drugs simply retard bacterial growth; their ultimate destruction is due to local and general immunity as previously defined. (See Chapters 4 and 5.)

cytic action and to humoral effort. Local immunity is the result of phagocytosis by a large group of mesenchymal cells, such as the heterophile leucocytes, the fibroblasts, the monocular exudate cells, the polyblasts or histiocytes, and the pericytes. A local humoral, immune substance (whose nature is unknown) has also been thought by some to aid in local immunity. General immunity is the result of both humoral and cellular forces. The latter are included in the great group of phagocytic cells known as the reticulo-endothelial system. It has been found in the experimental animal (see Chapter 4) that in staphylococcic septicemia trypan blue will not appear at a superficial site of local injury. This is due to peripheral vasoconstriction. The reticulo-endothelial cells and polymorphonuclear leucocytes are being used in more vital central areas. This explains why local immunity and fibroplasia are retarded in the presence of a septicemia.

The blood cells, such as polymorphonuclear and mononuclear leucocytes, and that group of general immune substances known as antibodies, and designated variously as agglutinins, bacteriolysins, precipitins, alexins, antitoxins, and opsonins, constitute the humoral forces that are available for effecting a general immunity to disease.

Explants from the spleen, the lungs, or the bone marrow of embryonic or adult laboratory animals are incapable of synthesizing precipitins, agglutinins, hemolysins, antitoxins, or complement-deviating antibodies. If antigens are injected into the living animal and an interval of two to three days allowed, then antibodies of high titer may be found in various organs. This tends to prove that *antibody production is the result of preparatory reactions produced by the body as a whole.*

Mackay and Menkin and others have shown that insufficient amounts of vitamins A and C may decrease the immunological panel.

In all probability these different types of immunity are very closely related and respond synergistically when needed. However, we have ample proof that local immunity can take care of a great many infections unaided (see Chapters 4 and 5). We may summarize by saying that this constitutional state broadly termed immunity is the sum total of the factors just mentioned. These are the actual scientific units in the immunologic panel. Why one person has an active well-trained reticulo-endothelial and antibody system and another an ill-trained, inactive one, we do not know. How to know which person has and which has not can be partially determined by panel types, various skin and serological tests, and blood counts, which we have described in previous chapters.

In infections that are localized, the very fact that they have localized and have not overwhelmed the patient bears evidence of good resistance. *Inflammation* due to pathogenic bacteria and *immunity,* whether local or general, are not the same thing. If we could artificially wall in an infected area by an inflammatory zone, it would not necessarily cure the patient or prevent a general septicemia or the occurrence of other infections "next

assortment as well as other generalizations. He found, for example, that *by crossing a pure red-flowered with a pure white-flowered pea plant* that the red-flowered plant appeared—no pinks or whites. Yet in subsequent generations white appeared. Thus he spoke of redness as dominant and whiteness as recessive. If the red offspring was self-fertilized, the resulting generation would be three-fourths red and one-fourth white. *If now there is an absence of dominance in the offspring between red* and white, that is, pink, then after self-fertilization in this flower the next generation will be one-fourth red, one-half pink, and one-fourth white. The unit characters have been separated and redistributed. This is known as the principle of segregation. As in plants, so in man, the in*dividual is an aggregation of more or less independent and separable* "unit characters," each of which is distinct and may exist in all sorts of combinations. Moreover, these traits exist in hybrids as contrasts: red and white, tall and short, etc. Such pairs of characters are called *allelic* pairs, one being the allele of the other. This is well exemplified in *the heredity of blood groups which we shall discuss later.* The principle of independent assortment assumes that "the relation of each pair of different characters in hybrid union is independent of the other differences in the two original parental stocks." Sinnott and Dunn have used the following example:

> Assume that of all the men in a given country half are brown-eyed and half are blue-eyed and that half are right-handed and half are left-handed. Assume further that there is no connection between these two characters so that of the brown eyed men approximately half are right-handed and *half* are left-handed, and of the blue eyed ones, the same. There will thus be four kinds of male individuals in about equal numbers. . . . Finally assume that the women are divided in just the same way and that *in determining what matings shall take place between men and women, eye color and* right-handedness and left-handedness play no part whatever. . . . The existence of four types of men and four types of women in about equal numbers will then result in 16 kinds of matings, although as far as actual appearance goes, there will be only four kinds of individuals. Therefore, the *genotype* (the germinal make-up of the individual; *the basic complex of genes) is not always apparent by outward appearance.* The *phenotype* as we have seen is the individual resulting from the interreaction of the parental genes; his appearance depends on dominant factors but he still harbors recessive factors as well.

HEREDITY IN BLOOD GROUPS

We are familiar with the blood groups, O, A, B, and AB—these are phenotypes. Due to the fact that certain genes are dominant over others, any given phenotype may be the expression of one or more genotypic pattern. In blood groups there are three allelic genes: A, a^B, and a. The first two (A and a^B) are dominant over the third (a) but are not dominant over each other. The gene A is responsible for the blood group A, a^B for group B, *a for group O, while the presence of both genes A and* a^B produce group AB.

This is the philosophy that governs the physician in his treatment of infection. It may sound like therapeutic nihilism; actually, it is simply the application of sound medical and surgical principles when infection occurs. It is a revival of Jonathan Hutchinson's dictum: "It is more important to know the patient than his disease." Consideration of the patient as a whole is necessary for successful care and cure.

HEREDITY AND THE HUMAN CONSTITUTION

Individuals tend to resemble their ancestors closely; this resemblance is called *heredity*. When the sperm units with the ovum (gametes) to form one fertilized cell (zygote), a new individual develops. In the elements of these cells reside the potential characters of the offspring. The anatomical pattern (color, eyes, skin, hair, size, shape, and body proportions), immunological pattern (susceptibility to defects and disease), physiological pattern (chemical peculiarities of blood and tissues), and psychological pattern (mental traits and capacities) are all inherited. True enough, variations occur. Practically no two individuals are exactly alike even though their resemblance is extremely close in every way. The science of genetics is a study of the phenomena of inheritance and variations. It attempts to formulate laws which govern similarities and differences between people related to one another by descent.

Variations occur in some panels because of environment. This is especially true in the psychological behavior of an individual. However, acquired characteristics are not transmitted as such.

Acquired characteristics are not transmitted, notwithstanding Lamarck's doctrines. An acquired character is one that has developed in the course of the life of an individual in the somatic or body cells, usually as a direct response to some external change in the environment or through the use or disuse of a part. Therefore, acquired immunity is not hereditary. Is it, then, the inheritance of a particular type (lateral) which affords a strong immunological panel? While this is true in general, the fact remains that certain races (composed of both linear and lateral types) have a strong immunity against certain diseases. Perhaps this may be explained by the modern conception of Darwin's pangenesis; namely, that the units of heredity already present may be modified by late contributions from other parts of the body and such modifications may be inherited.

Occasionally an individual will be found who differs greatly from his forebears for reasons as yet unknown. He is not only different himself, but he transmits his differences to his descendants. Such a new variation is known as *mutation* and is observed not infrequently in animals and plants as well as man.

Mendel's laws of inheritance were formulated by counting the numbers of each type of progeny resulting from a given cross and furthermore each trait or *character* of the pairs and their offspring. He was able thereby to formulate the principles of *segregation* and *independent*

In cases of disputed paternity it is not possible to say definitely that a child is the offspring of certain parents, but in some cases it is possible to affirm that the child is not their offspring.

HEREDITY IN CONGENITAL MALFORMATIONS

It is perhaps erroneous to assume that all congenital malformations and deformities are hereditary. Some are definitely so and may behave as dominant or recessive. Among the former may be mentioned telangiectasis and hypospadias and among the latter a score of abnormalities including albinism, harelip, certain types of blindness, anomalies of the gastrointestinal tract, etc. As is well known, hereditary traits are determined by genes carried in the chromosomes of the nucleus. Every individual receives two of every type of gene—one from each parent. In a simple dominant condition if one gene is defective it will appear on an average of one of every two offspring. In a simple recessive condition a pair of the same genes is required for the defect to show up in the individual. If the child receives a defective recessive gene from one parent, he will be normal but will be a carrier. If two carriers who are normal mate, a defective child will appear one in four times. If a defective parent and a carrier mate, the defects will appear once in two times. If both parents are recessive defectives, all children will be defective.

Sonneborn has shown that in the paramecium there may be a very different genetic system: the hereditary traits may be determined by nuclear genes in some of the species but in others they may be determined by the cytoplasm. He called these cytoplasmic factors *plasmagenes* because like genes they are self-reproducing and control the characteristics but unlike the genes they are located in the cytoplasm instead of the nucleus. They are, however, partly dependent for their maintenance and reproduction on the nuclear genes. Just what role these *plasmagenes* play in human heredity has not been determined. Perhaps chemical, virus, and other carcinogens induce mutations in plasmagenes which are more readily affected. The long period that normally intervenes between the application of carcinogenic agents and the visible development of cancer in experimental animals may be due to the fact that during this period the cellular concentration of the plasmagene is slowly increasing up to the critical level for cancer manifestation.

Murphy has made an exhaustive study of the incidence of congenital malformations in families. He believes that these arise from influences which affect the germ cells prior to fertilization. Other observations were: about one-fourth congenitally malformed are stillbirths, they are twice as common in whites as in Negroes, they are twenty-five times greater in families already having a malformed child. The older mother, the later-born rather than the first-born, long periods of sterility, all point to the occurrence of defects.

Since two genes, one contributed by each parent, interreact to produce the phenotype, Table VIII shows the genetic constitution responsible for any one of the four blood groups:

TABLE VIII

PHENOTYPE (BLOOD GROUP)	GENOTYPE
AB	Aa^B
B	a^Ba^B *or* aa^B
A	AA or Aa
O	aa

TABLE IX

BLOOD GROUPS OF PARENTS			POSSIBLE BLOOD GROUPS OF CHILDREN	IMPOSSIBLE BLOOD GROUPS OF CHILDREN
Phenotype: O × O	Parents:	aa × aa		
Genotype involved:	Children:	aa	O	A, B, AB
Phenotype: O × A	Parents:	aa × AA or Aa		
Genotype involved:	Children:	Aa or aa	A, O	B, AB
Phenotype: O × B	*Parents:*	*aa* × a^Ba^B *or* aa^B		
Genotype involved:	*Children:*	*aa or* aa^B	B, O	A, AB
Phenotype: O × AB	Parents:	aa × Aa^B		
Genotype involved:	Children:	Aa, aa^B	A, B	O, AB
Phenotype: A × A	Parents:	AA or Aa × AA or Aa		
Genotype involved:	Children:	AA, Aa or aa	A, O	B, AB
Phenotype: A × B	Parents:	AA or Aa × a^Ba^B or aa^B		
Genotype involved:	Children:	Aa^B, aa^B or Aa, aa	O, A, B, AB	None
Phenotype: A × AB	*Parents:*	AA *or* Aa *or* Aa^B		
Genotype involved:	*Children:*	AA, Aa, Aa^B *or* aa^B	A, B, AB	O
Phenotype: B × B	Parents:	a^Ba^B or aa^B × a^Ba^B or aa^B		
Genotype involved:	Children:	a^Ba^B, aa, aa^B	O, B	A, AB
Phenotype: B × AB	Parents:	a^Ba^B or aa^B × Aa^B		
Genotype involved:	Children:	Aa^B, a^Ba^B, aa^B, Aa	B, A, AB	O
Phenotype: AB × AB	Parents:	Aa^B × Aa^B		
Genotype involved:	Children:	AA, Aa^B, a^Ba^B	A, B, AB	O

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Phenotype: O × O				
Genotype involved:	Parents:	aa × aa		
	Children:	aa	O	A, B, AB
Phenotype: O × A				
Genotype involved:	Parents:	aa × AA or Aa		
	Children:	Aa or aa	A, O	B, AB
Phenotype: O × B				
Genotype involved:	Parents:	aa × a^Ba^B or aa^B		
	Children:	aa or aa^B	B, O	A, AB
Phenotype: O × AB				
Genotype involved:	Parents:	aa × Aa^B		
	Children:	Aa, aa^B	A, B	O, AB
Phenotype: A × A				
Genotype involved:	Parents:	AA or Aa × AA or Aa		
	Children:	AA, Aa or aa	A, O	B, AB
Phenotype: A × B				
Genotype involved:	Parents:	AA or Aa × a^Ba^B or aa^B		
	Children:	Aa,^{B} aa^B or Aa, aa	O, A, B, AB	None
Phenotype: A × AB				
Genotype involved:	Parents:	AA or Aa or Aa^B		
	Children:	AA, Aa, Aa^B or aa^B	A, B, AB	O
Phenotype: B × B				
Genotype involved:	Parents:	a^Ba^B or aa^B × a^Ba^B or aa^B		
	Children:	a^Ba^B, aa, aa^B	O, B	A, AB
Phenotype: B × AB				
Genotype involved:	Parents:	a^Ba^B or aa^B × Aa^B		
	Children:	Aa^B, a^Ba^B, aa^B, Aa	B, A, AB	O
Phenotype: AB × AB				
Genotype involved:	Parents:	Aa^B × Aa^B		
	Children:	AA, Aa^B, a^Ba^B	A, B, AB	O

pagos, joined) indicates a union ventrally of the chest and belly. This may imply a communication between thoracic and abdominal cavities with a single organ or double organs supplying the monster (*monere*, to warn; or *monstrare*, to indicate).

The modern theories of the cause of monsters and anomalies are described as developmental inhibition or arrest. Each organ not only originates from a definite embryonic area or primordium and from no other, but also it arises at a definite moment that must be utilized then if ever. Also if one organ is out of time others also are thrown out. Interference with the fetus in any way (ectopic, radiation, oxygen deficiency, lowering of temperature, slow rate of development) may produce anomalies.

Older theories included such intrinsic factors as vitality difference, fetal disease (local necrosis, improper physiological regulation), and interdependence of fetuses. Extrinsic factors were listed as direct (mechanical, physical, chemical, or transmitted disease) and indirect (environmental influences).

The role of heredity in anomalies is not entirely settled. Yet the occurrence of twinning and monsters in family lines transmitted equally often through the male or female makes the hereditary factor a very important one.

HEREDITY AND DISEASE

Many diseases appear in successive generations of a family: gallstones, goiter, varicose veins, hernia, appendicitis, hypertension, coronary disease, myopia, allergic diseases, hemolytic jaundice, peptic ulcer, "congenital" hypertrophic pyloric stenosis. and, above all, cancer. A familial incidence does not prove that a condition is hereditary nor does its absence prove that it is not. However, the knowledge that many *diseases are hereditary and moreover the potentialities of such diseases* are of great importance.

Some diseases are hereditary and behave as dominants (Huntington's chorea, paralysis, agitans, labyrinthine deafness, etc.). Some are recessive (diabetes mellitus, amaurotic idiocy, spastic paralysis, etc.), Some are sex-linked (hemophilia, color blindness, juvenile glaucoma).

The gene for hemophilia arises about once in 10,000 times in men and about once in 100,000 times in women. The usual sequence, then, is a mutation in the germinal tract of a man, whereby he has a carrier *daughter, the disease itself appearing when her son is born.* The fertility of affected males is less than one-third of the normal rate, so that genes for the condition are fairly well eliminated. Mutation and elimination balance each other so that the population is in equilibrium, with about 1 boy in every 7,500 boys being born a hemophiliac in Denmark. Andreassen demonstrated a delayed coagulation time in carrier women. This test can be used to assure the 50 per cent of the sisters of hemo-

Teratology (terato-logy, a telling of wonders) is the study of embryology that deals with abnormal development and its products; namely, anomalies. Normal individuals vary greatly from others of the same species as a whole and as to individual organs or parts. Great variations may occur in one individual or in twins. Twinning is in itself abnormal. Malformations are listed by Arey as follows:

1. Developmental Failure. The primordium may fail to appear or at least not develop to a significant degree. This is known as *agenesis*. Examples: absence of an arm or kidney.
2. Developmental Arrest. A transitory fetal state is retained permanently (cleft palate, imperforate anus, double uterus).
3. Developmental Excess. Growth is exaggerated or normal numbers are increased (gigantism, accessory digits, or mammae).
4. Displacement. Organs whether typical or supernumerary may occupy abnormal locations (transposed viscera, palatine teeth).
5. Fusion or Splitting. (Horseshoe kidney, cleft ureter.)

TWINS

If there is an independent fertilization and ripening of more than one ovum at a time, *ordinary* or *fraternal* twins are produced. They may be of the same sex or mixed and are not really twins. They resemble each other as do other brothers or sisters. When a single ovum develops into two or more individuals, they will be of the same sex and will have similar physical, mental, and pathological traits because each member acquires the same chromosomal heritage and therefore the same genetic constitution. These twins are known as *identical* or *duplicate*.

In single-ovum twins one individual may be normal in size and structure and the other less so or completely unable to exist as an individual after birth. Rarely they may be joined (double monster) by a small area of fusion or the entire bodies may be fused except the head or legs may be double. The former type (superficial union) may be separated surgically. When vital organs are divided both individuals may die or one may survive at the expense of the other—rarely both survive such procedure.

In otherwise normal persons one half may be larger than the other. This may be interpreted as a twin specimen with a minimal degree of doubling (Arey).

If there is a difference in size of the two components, the larger is called the *autosite*, the smaller the *parasite*. If the parasite is a perfectly included twin it is known as fetus in fetu. This is mentioned in Chapter 15 under teratoma, a tumor which includes parts of organs or almost the entire *parasite* within its capsule. Although the term *dipygus parasiticus* is often used to describe conjoined twins of different size, it is perhaps better to limit its use to those joined at the pelvis or lower part of the back (*dipygus*, double buttocks). Other terms are used when junctions are present elsewhere. *Gastrothoracopagus* (*gaster*, belly; *thorax*, chest;

abdominal cancers in kangri users; third, those due to medicinal agents (x-ray and radium and arsenic); fourth, those induced by chemicals in *occupations (arsenic, nickel, carbonyl, radium, mesothorium, asbestos,* mineral oils, pitch, tar, soot, paraffin oil, anthracene oil, creosote, aniline, naphthylamine, benzidine, benzene, all radioactive materials); fifth, a special miscellaneous group induced by parasites and virus. Internal and environmental factors include hormones, endocrine abnormalities, endocrine traits, inherited precancerous conditions such as necrofibromatosis, tuberous sclerosis, intestinal polyposis, xeroderma pigmentosis, and inherited metabolic abnormalities (hematoporphyrinuria from the sun makes skin more susceptible to tumors and it is itself a constitutional anomaly caused by light).

If there is a general susceptibility and an inherited favorable internal environment or if external environmental factors are present, such an individual may be a subject for cancer. In the latter instance the environmental factors may induce a predisposition to cancer. This subject will be discussed again in Chapter 15. The constitutional factors involved in cancer are varied and as yet not entirely known. However, here, as in infections, it takes two factors to produce the disease, the soil and the seed. Unlike infections, we know little concerning the seed (cause) and only a fragment more about the soil (resistance).

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philiacs who have not received the gene that they are not carriers and so can safely marry and have children, although its reliability cannot be considered as infallible.

In a large proportion of mental diseases and in diabetes mellitus, for example, environment plays a role as important as does heredity. In some instances the hereditary factor is known; for example, congenital polyposis of the colon. Its tendency to become malignant is also known. Therefore, here colectomy is definitely indicated as soon as the condition is discovered. Moreover, if it is found in one member of the family, it should be sought and eradicated in other members if present. The same may be said for retinoblastoma.

Cancer may be the result of heredity or environment or both. Undoubtedly cancer is not a unit disease so far as its *genetic behavior* is concerned. Tumors of different sites and types may show a strong hereditary factor or one in which it is possible but not sure, or there may be no suggestion of a hereditary factor at all. A high incidence of cancer in a family or families does not constitute statistical evidence for the heritability of cancer because of the frequency (one of every ten deaths) of the disease. By the law of probability it is bound to occur in a certain number of families and in twins. However, its occurrence in many such families and twins has been reported so commonly that it is certainly more than a coincidence, indicating the importance of heredity in the formation and localization of certain tumors, such as those of the colon, eye, breast and stomach.

Much research has been done on the genetics of cancer in animals. These studies include modes of transmission (species difference, general predisposition, localization, mendelian mechanism) and extrachromosomal (cytoplasmic) and milk-borne factors (in cancer of the breast). Since milk is the product of a portion of the cell's cytoplasm (apocrine gland, Chapter 22), perhaps the milk-borne factor is the plasmagene as described by Sonneborn.

There is much difference of opinion concerning the genetic behavior of cancer in animals. Slye believes that susceptibility and insusceptibility to cancer are unit characters involving one gene and that susceptibility behaves as a recessive and unsusceptibility as a dominant.

It is unlikely that a heritable spontaneous "cancer" condition exists in many and very improbably that one gene, dominant or recessive, is responsible for it if it does exist (Haldane).

It is better to speak of "inherited disposition" whether of refractoriness or susceptibility to tumor formation.

Environment, external and internal, plays an important role in susceptibilities. In the former group may be mentioned, first, those factors natural in the environment (arsenic in drinking water), solar cancers in dry sunny regions, bladder cancers in tropical regions where schistosomiasis is endemic; second, those due to habits (smoking, tobacco chewing,

Chapter 11

THE INTERCHANGE OF BODY FLUIDS

Approximately 55 per cent of the blood volume is made up of plasma and 45 per cent is made up of cells. The blood circulates within the vascular system in what might be termed three types of vessels: the large arteries and veins (vessels of storage), medium arterioles and venules (vessels for distribution), and the smal capillaries (vessels for interchange of oxygen, food, and waste products). Of the three types the capillaries are all important in the regulation of water balance. The capillaries are made of a single layer of endothelial cells, about 0.8 micron thick (less when dilated) and permit an exchange of food, water, electrolytes, oxygen, carbon dioxide, waste products, etc. However, this free passage through the capillary wall is possible only to crystalloids (inorganic salts, glucose, etc.) which are in true solution (solutes) in blood plasma; it is less possible to colloids (of which the most important are the solute proteins: serum albumin, serum globulin, and fibrinogen, totaling 6 to 8 Gm. per 100 c.c. of blood) because to these substances the capillary wall is normally impermeable, especially in the periphery of the body where plasma volume maintenance occurs. In the central viscera (lungs, liver, and visceral lymph) capillaries are almost as permeable to serum albumin as to crystalloids so that about half of the serum albumin is in the interstitial spaces. These colloids and crystalloids constitute a pulling force, which if unopposed would drain the intercellular fluid into the capillaries. However, it is offset by the hydrostatic pressure within the capillaries which constantly exerts an outward force. Therefore, the fluid within the capillaries is between two forces: the osmotic or "pulling" force and the hydrostatic or "pushing" force (Starling's theory). The same forces also affect the movement of the intercellular fluid and, to a lesser extent, of intracellular fluid.

The fluid structure of the body consists of three parts: the blood, the intracellular fluid, and the interstitial fluid, the sum of which constitutes about 70 per cent of body weight. This is divided as follows: the volume of circulating blood plasma is approximately 5 per cent, interstitial fluid comprises about 15 per cent, and intracellular fluid about 50 per cent of body weight. The interstitial fluid which includes the lymphatics is the most labile of the three, for in order to preserve contact with the other two it must undergo a constant shift in amount and, to a less extent, in electrolyte content.

Since on the arterial side of the capillary loop the hydrostatic force is greater than the osmotic, there is a passage of fluid outward into the

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the ameba, has a porous wall and therefore can absorb particulate matter. Blood cells, in general, are easily affected by their environment: hypertonic solutions produce crenation; hypotonic solutions, swelling. Cells in the mucous membrane of the bowel and in the tubules of the kidney have a selective action: in the intestine these cells may refuse or select protein; in the kidney, water and glucose are reabsorbed. Therefore, the cell, while dependent upon the intercellular fluid and oxygen for its survival, is not governed entirely by the mechanical principles advanced under Starling's theory—it has in addition a *vital selective and secretory power*. The water content of the cell is mostly *free*, that is, not *bound* by colloids, and is given up easily when needed.

DIAGRAM SHOWING THE MOVEMENT OF WATER BETWEEN BLOOD AND TISSUES*

	BLOOD ARTERIAL SIDE	TISSUE FLUID	BLOOD VENOUS SIDE	
Hydrostatic pressure	30 mm. Hg	8 mm. Hg	15 mm. Hg	
Osmotic pressure	25 mm. Hg	10 mm. Hg	26 mm. Hg.	
Effective hydrostatic force	22 mm. Hg		7 mm. Hg	
Effective osmotic force	15 mm. Hg		16 mm. Hg	
Hydrostatic in excess of osmotic	7 mm. Hg→	Fluid out to tissues Fluid in to vessels ——→	9 mm. Hg	Osmotic in excess of hydrostatic

*From Best and Taylor: The Physiological Basis of Medical Practice, Baltimore, 1937, Wm. Wood & Co.

Fig. 95.

Osmosis, Oncotic Pressure, Dialysis.—The osmotic pressure may be defined as the attracting force exerted by crystalloids and colloids in the capillaries. The actual pressure developed is supposed to result from the bombardment of the walls of the capillaries by imprisoned molecules of the dissolved or suspended substances. The permeability or semipermeability of the capillary wall is an essential factor in the development of the osmotic pressure. Since the capillary wall is normally less permeable to colloids, these substances exert a sustained osmotic pressure. The oncotic pressure is the osmotic pressure of colloids. Crystalloids, on the other hand, pass through the capillary wall readily and therefore they can exert an osmotic pressure only temporarily when a sudden change in concentration of these substances is introduced within the lumen of the capillary. The behavior of the tissue cells as has been stated is also affected by this process of osmosis. For example, the red blood cells are impermeable to potassium, sodium, and calcium, but they are permeable to water, chlorides, and bicarbonates. This will be discussed in the next chapter when we study the chloride shift.

tissue spaces. By the time the blood has reached the venous side of the loop, the hydrostatic force has fallen and the osmotic force has slightly increased (due to loss of water from the blood) and therefore the flow is from the tissues toward the vessels. Apparently the entire mechanism is a mechanical one and does not involve any selective action on the part of the vessel wall. The interchange of fluids is quantitatively expressed in the accompanying diagram.

In Chapter 17 we shall learn that lymph is composed of the intercellular fluid with some cells and particulate matter. Tissue fluid is forced into the permeable lymph vessels entirely by the hydrostatic force in the tissue spaces and the lymph vessels carry back to the blood stream such proteins as are not readily absorbed by the cells. The passage of water in and out of tissue spaces is probably intermittent. The spaces are artifacts; there are no lacunae in the tissues and no brownian movement has been observed (Freeman).

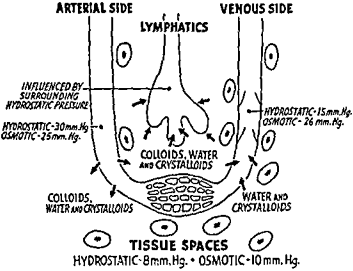

Fig. 94.—Diagram illustrating Starling's theory of the interchange of fluids. The effective hydrostatic pressure on the arterial side of the capillaries is 7 mm. of Hg; therefore fluid goes out into the tissue spaces. The hydrostatic pressure is reduced on the venous side and the osmotic pressure is increased because the blood has been concentrated by loss of fluid. The effective osmotic pressure is about 9 mm. of Hg, and water and crystalloids are absorbed. The permeable lymphatics absorb colloids as well as crystalloids and are influenced by the tissue-space hydrostatic pressure (muscular contraction, arterial pulsation, motion) although their colloid content exerts a small osmotic pull as well. The diagram represents a capillary loop and small collaterals.

The last and most important fact to be considered is the behavior of the intracellular fluid. Of this, little is definitely known. However, we do know that it varies with the type of cell. In unicellular organisms a single cell carries on all the functions necessary to the life of the animal. In higher animals different groups of cells have different functions. All cells are affected by their environment (tissue fluids and oxygen) and respond more or less to alterations in this environment. The mechanism by which they absorb foodstuffs is probably dialysis. The cell assimilates single molecules and synthesizes them into the complex substances which constitute its protoplasm. The macrophage, like

blood plasma. Plasma proteins are lost continually in varying amounts but are returned to the blood by the lymphatics. Capillaries are constantly being traumatized and repaired in part by the circulating fibrinogen which is converted into fibrin.

Within the capillaries are the red blood cells with a total surface of 30,000 square feet or nearly 3/4 acre. The great area of filtration which the capillaries possess is not easily described. Their permeability is such that the entire plasma volume could be filtered within ten seconds at a capillary pressure of 10 mm. were it not for the vasomotor action and the osmotic pull within them and the tissue space pressure around them. Capillary permeability is increased by many factors, it is decreased by none according to Krogh. However, he admits the possibility in citing Isayama's work on the loss of fluid from the frog's blood. After trauma by the cautery to the lymph hearts there is a latent period of six minutes before fluid loss begins. If fluid is lost between the endothelial cells more easily when they are separated, then a priori they should be lost less easily when approximated. The following is a list of some of the factors influencing capillary *permeability:*

A. Increased
   1. Inflammation
   2. Prolonged application of heat
   3. Anoxia
   4. Scurvy (vitamin C deficiency)
   5. Trauma
   6. Capillary poisons
   7. Allergy
   8. Vasodilation from nervous or other factors

B. Decreased
   1. Vasoconstriction

Osmotic Pressure Within the Capillaries.—The osmotic pressure of a solution of any pure substance depends upon the number of molecules, ions, or other particles which are present, irrespective of their kind or size. The osmotic pressure of a solution containing a mixture of substances is made up of the partial pressures of the single substances; that is, each substance acts as if it were alone, unless its free particles are modified by the presence of the others. The osmotic pressure of the blood is due mostly to inorganic salts and organic materials dissolved in the plasma. Starling showed that the proteins, which make up practically the whole of the colloids, have a definite though small osmotic pressure. The *osmotic pressure of the crystalloids cannot be continuously effective in normal capillaries because their walls are permeable to these substances. The osmotic pressure of the colloids is effective because of the relative impermeability of the capillaries to them.*

Probably the three proteins do not exist in the blood as separate and distinct substances but are bound together into a single complete substance, which is disrupted into its constituents by different agencies. Serum albumin amounts to 4.4 grams per 100 c.c. Its osmotic pressure is 5.5 mm. per gram or 24.2 mm. The albumin fraction contributes 85 per cent of colloidal osmotic pressure (1) because its molecular weight is the smallest and (2) because its concentration is twice that of globulin. The pressure which each protein fraction exerts is inversely related to its concentration in the plasma. Serum albumin is in the highest concentration and its molecule has the least

The term dialysis implies the separation of crystalloids and colloids in solution by means of *their unequal diffusion* through a natural or artificial membrane. Plasma exerts an osmotic pressure of about 25 mm. of mercury against a semipermeable membrane with isotonic salt solution on the outside. Five millimeters of this pressure difference are due to the unequal distribution of electrolytes in accordance with Donnan's law, which is discussed later in the chapter, and 20 mm. of mercury are due to plasma proteins. Serum is chiefly defibrinated plasma and *therefore it contains albumin and globulin but no fibrinogen.*

Colloids, Crystalloids.—The word colloid is derived from the Greek meaning glue and was originally introduced by Thomas Graham. He divided all substances into two classes; namely, *crystalloids,* including such substances as salt, sugar, urea which could be crystallized with ease, which diffused rapidly through water, and were capable of diffusing through dead animal membranes, and *colloids,* which included substances such as gelatin, gum, egg albumin, starch, dextrin, which were noncrystallizable, formed gummy masses when their solutions were evaporated to dryness, which *diffused with extreme slowness* through water and would not pass through animal membranes. At present these criteria do not hold, because *proteins can be obtained in crystalline form and different* colloids have different gradients of diffusion. Colloids exist under two *conditions:* (1) in a state of solution or *pseudosolution in which they* form sols and are designated as hydrosols when the solvent is water; (2) in a solid state in which a relatively small amount of the colloid sets with a large amount of fluid, such as water to form a jelly. This solid form, that is, gelatin, is known as a *gel.* Such a watery jelly is known as a hydrogel.

The Capillaries.—The capillaries form an enormous filtering area which is said to be 6,800 square feet or a thin membrane one yard wide and four miles long. Their total length is about 100,000 miles. The capillary walls are so thin that it would take about 30,000 to make an inch. They are a continuous tube branching repeatedly and being exposed directly to the tissue fluids, oxygen, and carbon dioxide. In the normal person they are continually dilating or contracting to diminish *or increase the supply of blood.* Hydrostatic pressures within the capillaries change some but osmotic pressure varies only slightly and *temporarily under normal conditions.* There is *great* variation in capillary permeability in different parts of the body.

The pleural capillaries are *most permeable, then the peritoneal,* then the cerebrospinal, and the least permeable are the subcutaneous. This same variation occurs in *different organs; the liver* where capillary endothelium is partly discontinuous loses most protein, the kidneys less than half as much. *Obviously interstitial fluid will vary in protein content* in these regions, that of subcutaneous tissues being 0.1 per cent protein, the kidneys, 3 per cent, and *the* liver, 7 per cent, or *equaling*

is best supplied by animal proteins, although their ingestion does not result in an immediate increase in plasma proteins which must first be synthesized by the liver. In disease the reserve supply is the principal source. This is important because a patient may have normal plasma protein fractions with the reserves exhausted. After surgery when protein is needed there is nothing to draw upon and hypoproteinemia results. The body can synthesize all amino acids into protein, but it cannot form amino acids except glutamic, alanine, and arginine.

Some of the so-called nonessential amino acids are provided by the synthetic action of bacteria in the large intestine. This is also true of the synthesis of vitamin K_2. When Sulfasuxidine or other intestinal chemotherapeutic agents are used these bacteria become inactive and this important source for preformed amino acids and vitamin K is removed.

The proportion of protein allocated to the liver, blood serum, and kidney is increased as the amount ingested is increased. The liver is enriched quantitatively as well as functionally. This is demonstrated by hyperplasia, hypertrophy, and an increased content of protein per unit weight of tissue. During abstention from food the relative loss is greatest for the liver.

There is not much preformed plasma protein as such and therefore in hemorrhage and shock it must be supplied by intravenous injection until the liver can take hold. However, the instantly available protein together with that less readily available may total one to five times the circulating mass.

Synthesis and Interrelationship of Plasma Proteins.—Plasma proteins are not inert molecules like pectin or acacia. Most tissue proteins are constantly undergoing synthesis and degradation. In the liver more than half of the protein may be broken down and resynthesized in ten days. Labeled amino acids appear within one hour after their ingestion in plasma protein, indicating the rapid build-up of the latter.

Whipple states that there are three kinds of protein: (1) labile reserve readily available for serum protein regeneration; (2) dispensable reserve which is less available; (3) indispensable and fixed of the body cells which is never available. Plasma and tissue cell protein are in 'dynamic equilibrium.'' The dispensable reserves in cells of the liver and all over the body can pass readily into plasma and the reserve without loss of nitrogen. The indispensable proteins may receive contributions from plasma but the reverse is not true because fixed tissue protein cannot be utilized to form proteins of the plasma or liver. Thus a patient may be kept in nitrogen and weight equilibrium by the intravenous administration of plasma and glucose, permitting a build-up of tissue protein as well.

Elman found that the relation between plasma and body protein is 1:30; that is, for every gram of body protein lost or gained, 30 grams of tissue protein are lost or gained during starvation or feeding.

weight (70,000 to 75,000); therefore, it plays *the most important* part in maintaining the colloid *osmotic pressure*. Serum globulin (2.7 grams per 100 c.c.—its osmotic pressure is 1.4 mm. per gram or 3.7 mm.) has a larger molecular weight (150,000 to 190,000) and is present in lower concentration, and fibrinogen (*0.27 grams per 100 c.c.*) has the highest molecular weight (200,000) and the lowest concentration.

Colloid osmotic *pressure is increased due to an artificial increase in colloids, their increased* production, or *their relative* increase due to loss of water. Examples are:

1. Injection of substances with high osmotic index such as blood, plasma, serum, acacia, pectin
2. *Increase in fibrinogen and globulin in tuberculosis, pneumonia*, and other infections, *multiple myeloma*, and also in pregnancy. In the latter the increase is slight or actually reduced if accompanied by hypoalbuminemia
3. Dehydration

It is decreased as a result of diminished ingestion *of protein*, failure of absorption *or synthesis* of *ingested protein, increased loss of protein and relative decrease due to dilution.* Examples are:

1. Starvation
2. Sprue
3. *Hepatic insufficiency*
4. *Massive hemorrhage* (see Chapter 13)
5. Nephrosis
6. Shock (see Chapter 14)
7. Injection of large quantities of fluid intravenously

Since the osmotic pressure within the capillaries is due chiefly to plasma proteins, *it is* well that *we consider these substances with regard to their source, synthesis,* and interrelationship, *functions*, and their ultimate fate.

PLASMA PROTEINS

Source of Plasma Proteins.—Plasma *fibrinogen* and *plasma* albumin are formed exclusively in the liver. Plasma globulin is also formed in *the* liver, augmented *by the* reticulo-*endothelial* system and lymphocytes. The amino acids are selectively absorbed by *the intestinal tract*, not by the lacteals into the lymphatics but by blood capillaries directly *into the portal circulation*, and *synthesized* in the liver into the proteins and plasma protein building material. Some of this is placed *as* reserve stores of plasma proteins in the liver and in other tissues. The fully formed *and fixed* protein *in the* body *cells is not available for the* formation of plasma proteins. There is, however, a dispensable protein *reserve* in the liver and elsewhere which is available for this purpose. The replacement of *plasma* protein *is from two* sources: *exogenous from* ingested foods and endogenous from the reserve stores of plasma protein building material. Not all food contains indispensable amino acids. Milk, for example, *does not contain cystine, an amino acid* which cannot be synthesized in the body. Gelatin is rich in *glycene* but *does not* contain tryptophan and valine which are essential. The indispensable or essential amino acids are *as follows*: *arginine, histidine*, isoleucine, leucine, lysine, methionine, phenylalanine, theonine, tryptophan, *and* valine. Of these, tryptophan, lysine, histidine, and arginine cannot *be* formed from body stores and *therefore must* come *from* the diet which

grams. *This represents the catabolism of 18.75 grams of tissue protein* because each gram of nitrogen represents 6.25 grams of tissue protein; that is, tissue protein contains 16 per cent of nitrogen, or each gram of urinary nitrogen represents the deamination of 6.25 grams of protein. In normal persons 1.3 grams of nitrogen are excreted daily in the feces and 3 grams in the urine. When intake and output are equal, the individual is in *nitrogen equilibrium. A positive* balance indicates that nitro*gen is retained; this is seen in children, in pregnant women, and in adults* recovering from wasting disease or after muscular exercise. A *negative* balance means that output exceeds nitrogen intake.

After surgery the nitrogen loss may be up to 25 grams daily. Amino acid nitrogen of plasma falls during anesthesia. The relationship of tissue protein to water is 1:5. Therefore, a patient losing 25 grams of nitrogen is losing 156.25 grams of protein (25 × 6.25) or 781.25 grams of *tissue protein (156.25 × 5) per day. This is a loss of weight equal to* about 1.63 pounds per day of muscle tissue or its equivalent because wet tissue protein as indicated weighs five times as much as dry protein.

Dextrose spares protein breakdown by supplying adequate calories. Nitrogen balance cannot be obtained by protein alone. This is due to the fact that under such circumstances the excretion of nitrogen always exceeds intake even though the individual ingests protein to his full capacity. *The reason for this is that man cannot consume and digest sufficient* amounts of protein to satisfy energy requirements. He must draw upon stores of carbohydrate and fats. After these are exhausted, protein elements of his tissues are disrupted. The nonnitrogenous portions of the amino acid molecules are burned to make up caloric deficiency, and quantities of nitrogen derived from food and body protein are in consequence excreted. Nonessential tissue fat can supply calories even if dextrose is not given. However, in the postoperative patient the nitrogen loss must be met by exogenous sources.

HYDROSTATIC PRESSURE OF CAPILLARIES

The hydrostatic pressure within the blood capillaries is extremely important in health and disease. Since tissue pressures vary somewhat in different parts of the body, the effective hydrostatic pressure will also vary. In general it may be assumed that where tissue pressure is low, edema is most apt to occur.

The most precipitous fall in pressure occurs in the arterioles. Indeed the arteries with their high presssure are separated from the veins with their low pressure by the arterioles which have been called the "physiological tourniquet." The pressure fall from the aorta to the small arteries is about 20 mm. of mercury; from here to the capillaries, the drop is 60 mm. of mercury. This is due to the frictional resistance which occurs as blood from the large vessels passes through the many small arterioles whose sectional area is only moderately increased, resulting

A low plasma protein leads to great depletion of reserve and thus to liver damage which in turn impedes protein synthesis.

Hypoproteinemia

Liver Impairment ⟶ *Deficient protein Metabolism and reserves*

Impairment ⟵ Metabolism and reserves

Thus we see that plasma proteins represent but a small part of the total body protein and that they do not remain static but are interrelated with the protein of body cells. A normal balance results from the continuous ingestion, absorption, and utilization of protein fractions, and apparently the essential amino acids must be *ingested* at the same time for proper protein synthesis. Parenteral administration of protein hydrolysates are not effective because the selective action of the intestine is lost. Moreover, during the immediate postoperative period practically all of the nitrogen is excreted; and if there is insufficient carbohydrate, the parenteral amino acids lose their nitrogen and the carbohydrate is used for energy.

Functions of plasma proteins.—We have seen that proteins are necessary for the formation of plasma proteins by the liver. This organ is protected against chemical, toxic, and other injury and is able to regenerate liver cells only if it has an adequate supply of protein.

Certain amino acids have a lipotropic activity such as methionine and cystine (with choline) which restrict the intracellular deposition of fat and prevent subsequent fibrosis. This is the rationale for high protein diet with choline (together with vitamin B complex) in atrophic cirrhosis of the liver. See Chapter 22.

Serum albumin is most important in surgery because it is most often depleted due to the size of its molecule which can easily traverse damaged capillaries. It accounts for 85 per cent of the osmotic pressure and this is not entirely compensated by a rise in the other fractions when serum albumin is greatly reduced. Thus serum albumin may be low, serum globulin high, and the total protein normal in amount, but edema and anuria are apt to occur.

Globulin is important in immunity because antibodies and complement are made of globulin and the reticulo-endothelial system is its chief source. The clotting process of blood depends on globulin for fibrinogen, prothrombin, and thromboplastic substance—all are globulins. Fibrinogen can be measured in plasma but not in serum which is expressed from clotted blood or plasma. All of the plasma proteins contribute to the viscosity of the blood, which is said to be a factor in maintaining blood pressure, and they keep the corpuscles more or less adherent.

Fate of Proteins.—The daily urinary excretion of nitrogen in a person on a nitrogen-free diet but of adequate caloric value is around 3

fluids although it comprises only 15 per cent of the total volume of fluid. Its importance lies in the fact that it is the intermediary between the capillaries and the tissue cells. It is therefore the most labile of the three and subject to greater shifts during physiological needs (digestion, sleep, profuse sweating) and morbid states. In the latter it has been called the "buffer" or "cushion" since it may change greatly without alteration of the volume of blood or intracellular fluid.

Much remains unknown about this fluid. In fact, it has been called tissue space, intercellular, extracellular, interstitial fluid to designate it as an individual compartment which in fact does not exist as such but is only a potential "space" permitting its slow circulation together with lymph. Since the capillary wall is freely permeable to water and salts, these occur in about equal concentration on both sides. They are less permeable to proteins and therefore this fluid contains much less protein than the plasma. We have already noted the great variation of this protein content under the discussion of capillary permeability.

Not only is the volume of interstitial fluid subject to variation but to a lesser extent its electrolyte content. The latter is held to within narrow limits in all three compartments, but changes in water and electrolytes occur first in the plasma and interstitial fluid, thus protecting the intracellular fluid which is disturbed only in extreme morbid states.

This is all a part of what Cannon called homeostasis and even here isotonicity is maintained to preserve the integrity of the cell, for the interstitial fluid is the environment in which the cell lives just as was the sodium content of sea water when the first cells began to develop into multicellular organisms, although in the sea the hydrostatic pressure of the animal's cells or capillaries must be greater due to the pressure of the environmental water; and all of the capillary systems can be considered as being at the level of the heart (Krogh). In large aquatic animals, therefore, only a very low osmotic pressure is required to prevent filtration.

The source of interstitial fluid is the capillaries. Fluid moves, as we have seen, because of effective osmotic and hydrostatic pressures. It is returned to the capillaries on the same basis. Protein molecules and excess fluid are returned by the lymphatics which behave as semipermeable membranes dependent on hydrostatic rather than osmotic factors. Fluid in the tissue spaces moves due to muscle contractions and the pulsations of arteries and arterioles. It is lost from the body through the lungs (expired air), the skin (sweating), gastrointestinal tract (secretions and excretions), and the kidneys (urine). The various amounts lost are shown in the accompanying figures. In normal persons the first three (that is, lungs, skin, and gastrointestinal tract) are satisfied first; the water that is left is excreted by the kidneys. In this way the quantity of urine excreted is a reliable indication that other requirements for water have been satisfied provided, of course, that the kidneys are normal. Thus the kidneys act

in only a slight reduction in velocity. Frictional resistance is proportional to the square of the velocity. Therefore, the effect of the greatly increased surface in the arterioles will be to offer a very great resistance to the flow of blood through these vessels.

In the capillary bed pressure falls some and this fall continues to the right side of the heart. In addition, velocity is greatly reduced as blood pours into the "capillary lake." When the arterioles are dilated and more blood flows into the capillaries and veins the pressure in the arteries falls and that in the capillaries and veins rise. If the arterioles are constricted, the reverse occurs. The velocity is high in the arteries but is reduced by several hundred times in the capillaries. Although the capillaries have a very small lumen, their combined sectional area is 800 times greater than the cross area of the aorta. The rate of flow is inversely proportional to the transverse section of the capillary bed. This slowing of the blood flow provides for the interchange of gases and food and the elimination of waste products. If the velocity were not reduced, the frictional resistance would be so great as to cause a further precipitous fall in blood pressure. The slowing of the stream makes frictional resistance little and also tends to raise blood pressure because lateral pressure is inversely proportional to velocity. The rate of flow in the capillaries is subject to little change and therefore they fill up quickly when arterioles dilate, causing an increase in their hydrostatic pressure. Capillaries have no diastolic pressure because this pressure represents the load which the arterial walls are called upon to bear since they are essentially "storage vessels" and the resistance which the ventricular contraction must overcome to open the aortic valves. Since the systolic pressure falls much more than the diastolic peripheral to the arterioles, the two pressures tend to be equal.

The blood current picks up speed in the veins. This is due chiefly to the differences in vascular bed areas and provides for the return of the same quantity of blood to the right atrium as leaves the left ventricle in a given period of time. In the chapters on hemorrhage and shock (Chapters 13 and 14) we shall see that if any part of this closed system of tubes increases or decreases its capacity, the heart may be deprived of this exact balance, temporarily resulting in cardiac inadequacy.

Hydrostatic pressure in the capillaries may be *increased* by (1) vasodilatation of arterioles, (2) obstruction to venous return, (3) increased minute volume output of the heart, and (4) increased blood volume. It is *decreased* by (1) vasoconstriction of arterioles, (2) vasodilatation followed by stasis as seen in inflammations, (3) loss of blood volume with low blood pressure, and (4) decreased minute volume output of the heart.

TISSUE SPACES

We have discussed previously the water compartments of the body. The tissue space fluid is extremely important in the interchange of body

sium inside the cell in accordance with Donnan's theory. If potassium is found in large quantities in the blood or urine, cellular damage has probably occurred. Bicarbonate and phosphate are waste products but they are also important in acid base balance. (See Chapter 12.)

Should sodium be retained in the interstitial fluid, water would also be retained to any amount required so that a normal concentration of sodium would be present. Thus retention of water even to edema levels is a compensatory mechanism designed to protect tissue cells against great increases in electrolyte concentration. Therefore, if water alone is ingested it will be excreted in large measure by the kidneys unless there is an excessive amount of sodium in the tissue spaces; if physiological salt solution is ingested it will be retained or excreted, depending on its need. If salt is lost in excessive amounts or is not ingested, a sodium deficit would occur with loss of water even to a point of dehydration; again so that isotonicity would be maintained. Therefore, interstitial water volume varies with electrolyte concentration and the body can easily increase or decrease the water content through the action of the kidneys, skin, and lungs. Sodium is excreted chiefly through the kidneys.

Glomerular filtrate results from an excess of hydrostatic pressure in the glomerular capillaries over the combined osmotic and intraglomerular pressures (see Chapter 23). This continues in accordance with Starling's hypothesis until the osmotic pressure in the glomerular capillaries due to the concentration of plasma proteins is equal to the *effective hydrostatic pressure. Since the capillaries are usually impermeable* to these proteins, the filtrate contains no protein. The concentration of electrolytes in the filtrate is equal to that of arterial plasma.

In the efferent arteriole the plasma with proteins are much more concentrated (about 20 per cent) when they enter the capillary tuft about the tubules. Here 99 per cent of the water and salts of the glomerular filtrate are reabsorbed, leaving only 1 per cent of the total filtrate to appear as urine.

Perhaps an antidiuretic hormone elaborated by the pituitary gland regulates the reabsorption of water by the kidney tubules. Since the pituitary secretion may be affected by nervous stimuli and by changes in the composition of the blood transmitted to the gland through mediation of the central nervous system, an overproduction or underproduction of this hormone may decrease or increase diuresis in pathological states.

Of the 1100 Gm. of salt filtered off from the blood each day, only *about 5 to 10 Gm. appear in the urine. Ninety per cent of this* reabsorption is due to the increased osmotic pressure in the capillaries surrounding the tubule. The remainder is subject to hormonal control chiefly through the adrenal cortex (desoxycorticosterone). Other steroids such as esterone, progesterone, and tesotosterone play a minor role in this control. Thus an increased body need for salt may be met to a small extent by increased salt reabsorption, a decreased need by decreased reabsorption, resulting in an increase in salt in the urine.

as a compensatory apparatus for excretion of fluid just as the interstitial spaces are a "cushion" for its *storage*.

Should the osmotic pressure of interstitial fluid vary greatly, adjustments would necessarily occur within the cell which must be protected. Therefore, the extracellular fluid retains its isotonicity. *This is accomplished through the action of the kidneys.* Sodium and chloride are the most important electrolytes of plasma and interstitial fluid. Potassium is present in small quantities but is retained by the cells which are impermeable to cations. Sodium, therefore, remains outside and potas-

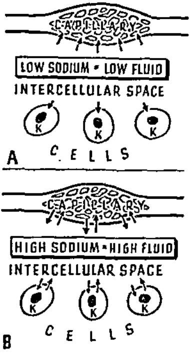

Fig. 96.—Intercellular fluid. The tissue spaces are extremely important in the interchange of body fluids, although they contain only about 15 per cent of the total volume of fluid. The importance of this fluid lies in the fact that it is the intermediary between the capillaries and the tissue cells; therefore it is the most labile of the three compartments; intravascular, intercellular, and intracellular.

The intercellular tissue space fluid has also been called the buffer or the cushion since it may change greatly and quickly without alteration of the fluid content in the capillaries or in the cell. No tissue spaces are actually present which are demonstrable. The space is probably a potential space permitting slow circulation of this fluid together with lymph. It has also been called the extracellular or the interstitial fluid space. *Since the capillary wall is freely permeable to water and salts, these occur in about* equal concentrations on both sides. Capillaries are less permeable to proteins and, therefore, there is less protein in the interstitial spaces than in the blood stream. The protein which is lost is picked up by the lymphatics and carried back to the blood stream.

The cell contains potassium and the interstitial spaces chiefly sodium. Potassium is retained by the cells which are impermeable to cations. Sodium, therefore, remains outside of the cell and potassium inside the cell in accordance with Donnan's theory. The filtration of fluid depends upon the effective osmotic or hydrostatic pressure as described in the text. Isotonicity must be maintained so that the cells may be preserved.

A. This diagram illustrates what happens when there is an absence or almost complete absence of sodium in the intercellular space. Should much fluid be present, it would become hypotonic, and, of course, the tissue cell would become plethoric and probably be damaged. Therefore, when sodium is low in the intercellular tissue space, fluid is lost so that isotonicity is maintained.

B. When sodium is high in the intercellular tissue space, much fluid is retained. Here again the purpose is to preserve the cell, and this is done through isotonicity. When sodium is present in excessive amounts in the *intercellular tissue spaces, water is retained* to preserve isotonicity and then water and sodium are lost through the kidneys. Should the kidneys be unable to excrete the excess sodium, fluid will be retained to preserve isotonicity, and edema *will occur.*

is able to diffuse freely into the majority of cells. However, in most instances the physical forces above described are insufficient to account for the exchange of substances. Krogh reports the problems raised by Heidenhain concerning the transport of calcium from the blood to the milk in the cow. "The cow produces milk at the rate of 25 liters a day, with a calcium content of 42.5 grams or 1.7 grams per liter. This *quantity of calcium is derived from the blood, in which the calcium content does not* exceed 0.18 gram per liter. The calcium ions cannot possibly move spontaneously from the blood to the alveoli of the mammary gland. Their transport must involve the expenditure of energy, must involve work performed in living cells by means of some special 'machinery,' so far utterly unknown, adapted for the purpose; must involve, in short, *secretion* of calcium."

Thus cells, in addition to their behavior as semipermeable membranes, enter actively into the production of products necessary to life. However, they are literally a fluid within a fluid separated only by the cell membrane. Therefore, they are susceptible to changes in their environment. Moreover, if the cell wall is damaged, their chief cation potassium is lost into the intercellular fluid, appearing finally in the urine in larger quantity than normal. This finding then may be an indication of cell damage, and it is understandable why changes in sodium concentration occur rapidly, whereas changes in potassium occur slowly. The term "available water" is only relative. When the blood needs fluid it is taken from the intercellular compartments. With the loss of fluid there is loss of electrolytes. These must be replaced or severe hyponatremia results, disturbing osmotic relations between cells and intercellular fluid. Intracellular water will be pulled out by the increase in ionic concentration in the intercellular fluid, thereby depriving the cell of its water. Exchange of gases will be disturbed due to stagnant anoxemia with resulting tissue anoxia. This in turn injures the cell wall, causing it to lose its cations (chiefly potassium), thereby further disturbing its metabolism. The loss of potassium from the cell ultimately results in hypokalemia due to increased excretion of potassium in the urine. The sodium content of the cell is then increased and serum bicarbonate is high to maintain biological equilibrium. *Chloride is excreted and bicarbonate retained. Potassium chloride* is necessary to increase intracellular potassium and lower intracellular sodium and to cause an increase in serum chloride and a decrease in serum bicarbonate.

Either inadequate intake or excessive loss of salt and water through the kidneys or gastrointestinal tract may produce this picture. Obviously the changes noted here in the cells are secondary to those in the blood. Plasma volume is greatly decreased; serum protein hematocrit and red blood counts are increased. Concentrations of sodium and chloride are decreased, while potassium is increased. If the dehydration is complicated by acidosis as in untreated diabetes mellitus, serum bicarbonate is decreased.

If vomiting occurs due to pyloric obstruction with loss of chloride, the blood becomes more alkaline and the concentration of blood bi-

In Addison's disease the control is lost but the mechanism remains intact. Here salt is lost and with it much extracellular fluid (see Chapter 22). If the glomerulus is damaged, as in acute glomerulonephritis, less salt will be filtered but the tubules take back their usual amount. This results in salt retention and edema. If both glomerulus and tubule are damaged, the effects will depend on which predominates. Tubule damage means salt loss with dehydration.

Tissue pressure is almost everywhere equal to atmospheric pressure except in the lower part of the abdominal cavity, where there is a positive pressure due to the weight of the intestines, and in the pleural cavity, where there is a negative pressure (see Chapter 14). The pressure in the pleural cavity is about 6 mm. of mercury (80 mm. of water) lower than atmospheric. The cause of this (Krogh) is that the pleural cavity is sufficiently resistant mechanically to allow definite pressure differences to occur. The colloid osmotic pressure of the blood is normally about 360 to 400 mm. of water, while the hydrostatic pressure in the capillaries of the pleural cavity and surface of the lungs is much less. "Therefore water will be drawn (with crystalloids) from the cavity into the blood and thereby expand the lungs of the newborn and keep them expanded thenceforward" (Krogh).

The hydrostatic pressure in the *tissue spaces* may be *increased* by (1) increased filtration from the capillaries from any cause, (2) obstruction to the lymph return, (3) increased osmotic pressure due to damaged capillaries, as in traumatic shock or inflammations, and (4) prerenal deviation of water and salt, due to the lag between ingestion and excretion of salt and to storage of water and salt in the skin and subcutaneous tissues. This may be due to increased activity of pituitary antidiuretic hormone from nervous or other causes.

The osmotic pressure in the tissue spaces is increased due to loss of protein through permeable capillaries or obstructed lymphatics.

Lymph.—The lymph capillaries help drain the tissue spaces (see Chapter 17).

An *increase in lymph flow* may be due to (1) increased intercellular pressure in the tissue spaces, (2) active motion, (3) passive motion and massage.

A *decrease in lymph flow* may be due to (1) decreased filtration of fluid from the capillaries, (2) obstruction of the lymphatics from lymphangitis, new growth, fibrosis, infection with *filaria sanguinis-hominis*, or familial lymphedema (Milroy's disease).

INTRACELLULAR FLUID

Most of the body's fluid is in its cells. We have already considered the elaborate precaution which nature takes to protect this fluid and the tenacity with which the cells hold on to it. Ionic concentrations on either side of the cell membrane must be the same for osmotic reasons.

The Donnan theory of membrane equilibrium predicts the distribution of ions which will take place on either side of a membrane which is impermeable to one of the ions. It has been used to explain the exchange of anions (chloride and bicarbonate) between the plasma and the interior of the red blood cell conditioned by the impermeability of the red cell membrane to sodium, potassium, and other cations.

In general, gases enter or leave cells by simple physical diffusion (although special mechanisms exist for the transport of oxygen and carbon dioxide in the blood). Urea

Salt.—Water is taken into the body as a matter of habit in America. Other liquids are substituted in countries where water supply is not as available or potable. Such liquids are chiefly wines diluted with water. The body is warned of the need for water by *the sensation of thirst. This* phenomenon according to Talbott, Dill and others is little understood. It depends on diminished water content and increased osmotic pressure of body cells rather than a dry mouth, although the latter may have a common origin with the former. Contractions of the smooth muscle of the esophagus may play a role.

A small increase in osmotic pressure produced by sodium chloride creates an intense thirst. Yet the ability to distinguish between a desire for salt and a desire for water is poorly developed in man although highly developed in animals. The normal individual uses about 5 Gm. of sodium chloride per day. The volume of sweat in eight hours of hard work in hot weather is said to be 10 to 15 liters and each liter contains 3 to 4 Gm. of salt. Therefore, water alone cannot satisfy thirst when both water and salt are lost. This is well known to those in hot climates or those who supervise the health of employees working in extreme heat in factories, boiler rooms, etc. Water alone without salt, as we have seen, leads to shrinkage of interstitial fluid volume, leading to dehydration in spite of water intake. Tropical languor characterized by weakness, fatigue, and anorexia in sedentary persons and muscle cramps in those engaged in hard work are evidences of salt deficiency, not water intoxication. Sometimes a shocklike syndrome occurs with loss of weight, weakness, apathy, anorexia, hypotension, orthostatic fainting, but there is *very little thirst* and an ample output of urine. Such individuals need 15 Gm. of salt daily with water. The excess NaCl will be excreted.

True dehydration consists of a great diminution of water without an associated loss of salt. This is a shortage of water in relation to solutes. Water is retained in the interstitial spaces for osmotic reasons (hypernatremia) and yields to the blood stream because of the osmotic pressure of plasma proteins. There is no hemoconcentration for some time; there is *severe thirst* and oliguria with azotemia. The kidneys do not excrete this excessive amount of salt. Such individuals need water. In clinical practice combinations are encountered. For example, an obstruction of the esophagus would lead to an absence of water, alone without loss of salt, whereas severe diarrhea, vomiting, intestinal fistulae, and Addison's disease cause a deficiency in electrolytes and water.

Salt Block.—The excessive parenteral administration of salt solution may bring about a condition known as salt block, which is characterized by *edema, anuria,* and *high fever,* followed in some cases by delirium and even death. Torbert and Cheney found a reduction in colloidal osmotic pressure of the blood serum after the ingestion of large amounts of sodium chloride (20 to 60 Gm. daily). The blood chlorides rise to high levels. Salt is more important than water because if salt

carbonate is increased. Later if the kidneys fail to excrete nitrogen azotemia results. This is late because the kidneys can make a hypertonic urine and may continue to excrete nitrogen products in a small amount of urine. Under these conditions, as we have seen, the tubules will reabsorb practically all of the sodium chloride. Finally with a decreasing plasma volume, flow through the glomerular capillaries is greatly diminished; blood viscosity is increased as proteins are concentrated; hydrostatic pressure is inadequate to form glomerular filtrate with resulting anuria.

Such a picture is not common in clinical practice where proper measures are introduced before this stage, which may take several days, has had a chance to occur. Since potassium is the chief cation within the cell, its depletion causes great changes inside and outside of the cell membrane. Hypokalemia may be caused by lack of intake in food, large amounts of glucose and saline infusion, vomiting, and the ingestion of ammonium chloride or the administration of testosterone. When intracellular potassium is reduced and intracellular sodium increased, biological equilibrium is achieved by a high serum bicarbonate and an increase in urinary chloride excretion. Thus alkalosis with hypochloremia and hypokalemia exist together. Gamble and co-workers showed that in order to keep the total milliosmols around 310 milliosmols per liter, potassium leaves when sodium is added. Therefore potassium and not sodium must be given.

The measurements of the osmotic features of extracellular fluid components are best stated in terms of ionic concentration. According to Gamble, the valency is disregarded. He suggests the term milliosmols per liter (milligrams per liter divided by atomic weight). Milliosmolar and milliequivalent values for the univalent ions are the same. The chemical equivalents of divalent ions are twice their milliosmolar value. Gamble suggests that the term milliosmolar be used instead of millimolar to make clear the osmotic effect of individual ions. In other words, the milliosmolar value of a solution of sodium chloride is twice its millimolar value. The normal value for ionic concentration of extracellular fluid as a whole is 310 milliosmoles per liter.

FACTORS AFFECTING THE NORMAL WATER BALANCE

Water is the most abundant constituent of the tissues and is taken up and released more rapidly than any other substance. When only 10 per cent of the body water is lost, serious subhydration occurs. Water is taken into the body by fluids drunk and by food eaten. Solid food is a source of water not only because most foods are about 70 per cent water, but also because in the process of oxidation of food in the body, water is formed. Even if no food or fluid is ingested, about 500 c.c. of water per day become available (during the first days of a fast) due to body tissue metabolism.

Adolph states that the daily water turnover is about four gallons. Since the stomach absorbs nothing (except alcohol) it must be looked upon as a storage tank for food and water, whereas the colon is an absorption system for the conservation of water. Phylogenetically these organs were designed to give man freedom in his environment. Since he can do without food due to fat and other deposits for longer periods than he can be without water, a method is provided for conserving the latter.

Although the vaporization process takes precedence, the kidneys will do their work with whatever fluid is available. If ample fluid is taken, the specific gravity of the urine will be low (assuming kidney function to be normal); if not, the specific gravity will be high. Therefore, a small quantity of highly concentrated urine (high specific gravity) means probably that insufficient water is being taken and that the body is maintaining a normal water balance. (Oliguria due to kidney damage or to ureteral obstruction should be ruled out by giving adequate amounts of water.)

The movement of water is intimately associated also with the distribution of electrolytes; the concentration of each ion is maintained through the retention or elimination of water. In the body fluids the chief basic ions are Na^+ and K^+ (sodium in extracellular fluids and potassium in intracellular), and the chief acid radicals are HCO_3^- and Cl^-. The sum of the basic ions must balance the sum of the acid ions. Loss of Cl^- can be made good by the retention of HCO_3^- and a rise in plasma bicarbonate. Excreted base can be *replaced only by basic substances supplied in the food or given parenterally.* The total concentration of electrolytes is therefore dependent upon the amount of base stored. Therefore, the body retains base. Acids are the products of metabolism and are excreted in large quantities. The kidneys compensate by altering the balance between sodium acid phosphate (NaH_2PO_4) and basic acid phosphate (Na_2HPO_4). On an ordinary mixed diet containing meat the urine is acid; that is, there is a relative excess of Na_2HPO_4. On a vegetable diet the urine is alkaline with a relative excess of Na_2HPO_4.

Whenever there is an excess of alkali in the body there is an increase in plasma bicarbonate, and base Na^+ or K^+) will be lost, for the urine will contain a larger proportion of Na_2HPO_4. Thus in dehydration due to pyloric obstruction, as Gamble has shown, glucose solution, water, or water with chlorine ions will not restore water balance; sodium chloride is needed. If there is an excess of acid, there will be a decrease in plasma bicarbonate, and radicals (HCO_3^-; Cl^-) will be excreted and the urine will contain an excess of acid phosphate (NaH_2PO_4). This is illustrated when base depletion is a primary cause of dehydration (biliary, pancreatic, or intestinal fistulae) or when as a result of dehydration the kidneys are impaired and do not reabsorb a sufficient amount of sodium. However, with acid or base there is increased diuresis

is retained (hypernatremia) water must be. *Water can be eliminated easily (skin, lungs, kidneys, intestinal tract).* Salt with sodium is *retained* when *given* intravenously after operation. Perhaps as in burns and other trauma, it is due to an increased tissue demand for salt, especially in the traumatized areas, and the inability of the kidneys to excrete it. With this salt much water is also retained in the interstitial spaces and is not available for vaporization, perspiration, and urine. If the normal person needs 5 Gm. of *sodium chloride per day and if 3,000* c.c. of physiological *salt solution is given intravenously, then 27 Gm.* of salt *are introduced.* This may lead to retention of salt which calls upon the intracellular fluid to maintain isotonicity in the tissues. Under such conditions edema is a protective mechanism. But the kidneys do not excrete salt in sufficient quantities to maintain isotonicity. Such salt retention leads to oliguria with more salt retention, more water bound, coming from the intracellular fluid with dehydration of cells and impairment of their *function, especially the brain, which is shown clinically by delirium and disorientation, and the kidney, shown by anuria. Coller* and associates recommend the infusion of hypotonic solutions *(0.45 NaCl* or 0.38 per cent NaCl plus 0.11 per cent $NaHCO_3$) postoperatively for forty-eight hours during the salt intolerance period. The administration of 5 per cent glucose in distilled water is specific, reducing the edema and restoring normal urinary function. It is probably the discontinuance of the salt and the adequate supply of water, rather than the glucose, that helps.

Movement of Water.—Water is lost by vaporization from the skin *to regulate the body temperature. Twenty-five per cent of the body heat is dissipated in this way (the other 75 per cent is lost by radiation,* conduction, and convection). *According to Newburgh, this 25 per cent* equals a loss of about 1,000 to 15,000 c.c. of water daily, *varying with* the need of sweating. Maddock and Coller assert that this water takes preference over water used by the kidneys. Kidney function is dependent on water intake. The kidneys excrete about 35 Gm. of waste material daily. If they function normally, they may accomplish this by the use of about 500 c.c. of water. Since kidney function varies with various activities in pathological states, this amount is usually inadequate. The average requirement is about 1,500 c.c. of water for excretion *daily. Of water that is ingested,* 70 to 80 per cent is excreted within *two hours, and about 25 to 30 per cent in half an hour.*

Lesser *amounts of water (about 300 c.c. daily) are lost* by the lungs, which aid in vaporization. *(In the dog there are no sweat glands and* vaporization is carried out almost *entirely through the lungs). About* 150 c.c. of fluid is lost in the feces normally. The reason *the amount is* small is that most of the 7 to 10 liters poured into the *gastrointestinal and* pancreatic juices and the bile is absorbed in the colon.

About 500 c.c. of bile are secreted daily 1,000 to 2,000 c.c. of gastric juice, 500 to 1,500 c.c. of saliva, 700 to 1,000 c.c. of pancreatic juice, 700 to 3,000 c.c. of intestinal secretion (succus entericus).

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because water moves with electrolytes and electrolytes move with water, leading to subhydration unless restored. Sometimes acid-producing salts are used as diuretics.

Clinical Application of Starling's Theory.—Let us now consider the application of Starling's theory in some physiological and pathological states. It is apparent that three factors must be borne in mind; namely, the effective hydrostatic pressure, the effective osmotic pressure, and the permeability of the capillaries. Since in many conditions more than one factor may be at work, it is often difficult to categorize such causes. Naturally one aberration leads to others. Therefore, we shall consider the primary factors in the discussion pointing out accessory or secondary effects as well.

Hydrostatic Pressure Changes.—Venous stasis produces edema not only through an increase in hydrostatic pressure, but also through an increase in capillary permeability brought about by stagnant anoxia. This is exemplified in the general edema of cardiac decompensation (although there may be kidney damage also, decreasing its functional capacity for sodium excretion), in the accumulation of fluid in the abdomen (ascites) due to portal hypertension as in cirrhosis of the liver (here leaky capillaries due to portal anoxemia play a role), in the face and neck upon obstruction of the superior vena cava from aneurysm of the aorta and mediastinal tumors, and in the legs from thrombophlebitis.

In cardiac decompensation with ascites the effective hydrostatic pressure in the abdominal veins is somewhat decreased due to the fluid in the abdominal cavity. In this way the veins are supported so that they do not continue to dilate. When ascitic fluid is suddenly removed, much dilation occurs with an increased pooling of blood and sometimes resulting shock.

In peripheral vascular disease obstruction to the veins or the lymphatics causes edema. The venules have an increased hydrostatic pressure.

This may be produced experimentally by the application of a rubber cuff to the extremity. Mende showed that when the pressure was raised to 100 cm. of water an increase in volume of about 40 c.c. took place. During the next fifteen minutes a further increase of 60 c.c. took place. This continued for a further period of twenty minutes when decompression took place after a total increase in volume of 120 c.c. On decompression the volume went down about 70 c.c. in two minutes and thereafter took thirty-five minutes to regain the original volume.

In hemorrhage there is a loss of blood volume. The hydrostatic pressure is reduced and the osmotic pressure is unchanged, so that fluid will be drawn into the blood stream. The concentration of the blood cells and of the protein will be lowered due to the space-filling effect of the migrated intercellular fluid, although more red blood cells would give a more permanent addition to the circulating blood volume.

In old people who are kept in the recumbent position for long periods, the venous flow is decreased because the venous return depends partially on muscular action. (Long inhalation anesthetics and spinal anesthetics have the same effect.) In addition, the hydrostatic pressure in the capillaries is decreased due to a pooling of the blood in the venules, which decreases the volume of the circulating blood. The arterioles contract to offset this and a shocklike state ensues. This may give rise to edema (due to increased permeability of capillaries from stagnant anoxia) or to thrombosis. (Pain in the extremities at night in patients with arteriosclerosis is probably due to an insufficient blood supply caused by a lowered blood pressure.)

Osmotic Pressure Changes.—In loss of fluid (anhydremia) by diarrhea, vomiting, excessive sweating, or excessive diuresis the blood plasma becomes concentrated and water is drawn into the blood stream. There is an increase in the concentration of the plasma protein as well as an elevation of the red blood cell count and as a result the blood is thick (hemoconcentration).

Saline cathartics cause water to enter the bowel because of the osmotic pull of the concentrated salt solution. In this way they draw water from the tissues. Postprandial thirst (a milder form of dehydration) is explained in the same manner.

"If the distribution of the absorbed water and crystalloids between the blood and the chyle is to be at all explicable as the result of simple osmotic processes, the concentration of each substance in the chyle must never be lower than in the blood, while the quantity of chyle flowing from the intestine per unit time must be at least somewhat higher than the corresponding quantity of lymph flowing from the empty gut." (Krogh.) If this is true, water will be drawn out of the capillaries surrounding the intestines, and diffusible substances will enter the blood stream. After complete equilibrium, the increased colloid osmotic pressure in the capillaries reabsorbs water from the intestine.

Shock is due to a loss of blood plasma into the injured area through traumatized and abnormally permeable capillaries. The loss of blood volume lowers the hydrostatic pressure; the loss of plasma protein lowers the osmotic pressure; the capillaries become packed with cells, due to the stagnation of the viscid blood. Capillary pressure rises and transudation of fluid is increased. If any fluid is absorbed from the tissues it is promptly lost from the capillaries in the injured area and thus a vicious circle is established. If large quantities of fluid are given intravenously, the hydrostatic pressure will be increased and more plasma will be lost with the fluid into the injured area, decreasing further the osmotic pressure; as a result water will leave the capillaries throughout the body, causing so-called "water intoxication."

In infections the capillaries become more permeable and plasma proteins exude together with inflammatory cells, at the site of inflammation.

Lewis believes that *inflammation* (as described in Chapters 4 and 5) is due to the liberation of *H-substance*, a *product of tissue cells that are exposed to injury of any kind.* The whole reaction is a defensive mechanism *which counteracts the injury without calling upon the central organization of the body.*

The osmotic pressure of the tissue fluid in this area rises until it equals that of the blood, so that absorption will not take place (Chapters 4 and 5).

Capillary Permeability.—Capillary permeability may be affected in such conditions as pernicious anemia, leucemia, angioneurotic edema, and Addison's disease but usually it is a combination of the factors mentioned which cause edema. This is seen in the cachectic states of carcinoma and late tuberculosis.

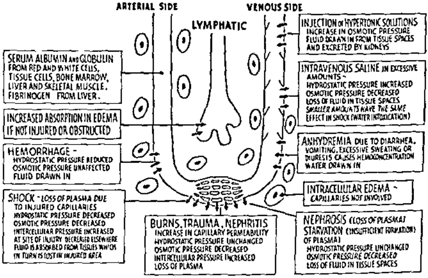

Fig. 97.—Diagram illustrating examples of interchange of fluid in abnormal conditions. A capillary loop and collaterals are represented; also a lymphatic capillary. Where plasma has been lost, it is necessary to supply this first before giving intravenous saline, so that the latter may be retained within the capillaries. Therefore a red blood count and hemoglobin determination should be done to determine the degree of hemoconcentration before intravenous medication is begun.

Edema.—Edema may result from an increase in hydrostatic pressure, a decrease in osmotic pressure, increased capillary permeability, or lymph blockage. We have considered all of these factors previously in relation to the three water compartments. Thus we may say that *edema* is an extrarenal phenomenon although the kidneys play an important role. However, even in acute glomerulonephritis the edema may be due to a general capillary disease. When both kidneys are removed in the experimental animal, edema does not develop. Water is removed by extrarenal means as it is normally. This amounts to 40 per cent of water excretion. Oliguria is the result, not the cause, of the edema. *Renal* edema is divided into two types: nephritic and nephrotic. *Nephritic* edema occurs in acute glomerulonephritis. It is due at least in part to an increased permeability of the capillaries because the edema fluid contains over 1 per cent protein. The capillaries of the *subcutaneous tis-*

sues are injured by the same toxins which act on the capillaries of the glomeruli. It is therefore an inflammatory edema. It may also be due to an elevation of hydrostatic pressure in the capillaries when there is an associated congestive failure. Nephrotic edema occurs in chronic nephrosis, the nephrotic stage of glomerulonephritis, and in amyloid kidney. The protein content of this edema is 0.1 per cent. This is due to loss of albumin principally, as shown by the reversed albumin globulin ratio. Chronic renal edema improves as the kidney becomes more impaired. This is due to the fact that less albumin is lost, causing blood proteins to rise, increasing osmotic pressure. A secondary cause of renal edema is the retention of sodium as previously discussed.

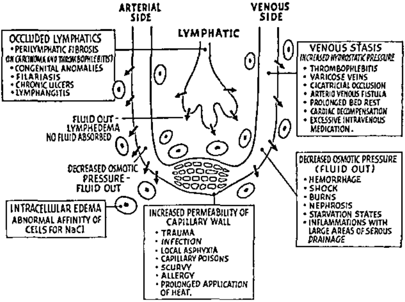

Fig. 98.—Diagram illustrating the mechanism of edema in the extremities. The arterial and venous sides of the blood capillaries are shown, also the lymphatic capillary. It is well to remember that more than one factor may be at fault. Not represented is the element of spasm, which occurs in both veins and arteries as a result of thrombophlebitis. This increases venous pressure, decreases arterial blood, and thereby further promotes anoxia with more permeability of the capillaries. Arterial pulsation normally aids in the movement of lymph, absence of pulsation retards this movement.

Dehydration.—When the output of water exceeds the intake, dehydration results. This may occur from insufficient intake of fluid and food, excessive loss of water, reduction in electrolytes, or the injection of hypertonic solutions. Maddock and Coller have shown that the greatest loss of fluids in the surgical patient occurs postoperatively, due to vaporization through excessive sweating. In addition, fluid is lost by vomiting and in the urine. Excessive fluid may be lost also in conditions with high fever (vaporization). Sweating occasions the loss of much salt as well and therefore may create a hypochloremia with alkalosis. Other causes which are not physiological (absolute losses) are blood loss, vomitus, drainage from intestinal and biliary fistulae, diarrhea, and massive exudation from inflamed surfaces (such as infections and burns).

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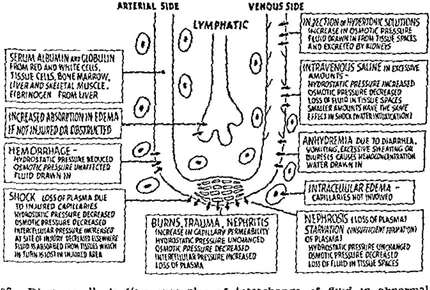

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sues are injured by the same toxins which act on the capillaries of the glomeruli. *It is therefore an inflammatory edema. It may also be due* to an elevation of hydrostatic pressure in the capillaries when there is an associated congestive failure. Nephrotic edema occurs in chronic nephrosis, the nephrotic stage of glomerulonephritis, and in amyloid kidney. The protein content of this edema is 0.1 per cent. This is due to loss of albumin principally, as shown by the reversed albumin globulin ratio. Chronic renal edema improves as the kidney becomes more impaired. This is due to the fact that less albumin is lost, causing blood proteins to rise, increasing osmotic pressure. A secondary cause of renal edema is the retention of sodium as previously discussed.

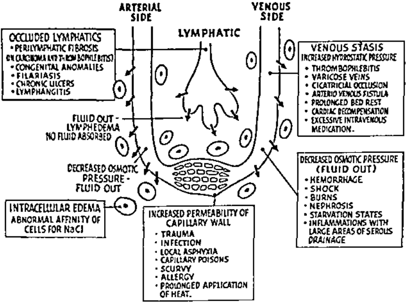

Fig. 98.—Diagram illustrating the mechanism of edema in the extremities. The arterial and venous sides of the blood capillaries are shown, also the lymphatic capillary. It is well to remember that more than one factor may be at fault. Not represented is the element of spasm, which occurs in both veins and arteries as a result of thrombophlebitis. This increases venous pressure, decreases arterial blood, and thereby further promotes anoxia with more permeability of the capillaries. Arterial pulsation normally aids in the movement of lymph, absence of pulsation retards this movement.

Dehydration.—When the output of water exceeds the intake, dehydration results. This may occur from insufficient intake of fluid and food, excessive loss of water, reduction in electrolytes, or the injection of hypertonic solutions. Maddock and Coller have shown that the greatest loss of fluids in the surgical patient occurs postoperatively, due to vaporization through excessive sweating. In addition, fluid is lost by vomiting and in the urine. Excessive fluid may be lost also in conditions with high fever *(vaporization). Sweating occasions the loss of much* salt as well and therefore may create a hypochloremia with alkalosis. Other causes which are not physiological (absolute losses) are blood loss, vomitus, drainage from intestinal and biliary fistulae, diarrhea, and massive exudation from inflamed surfaces (such as infections and burns).

Another example of dehydration is seen in diabetic coma. The important factor here is an excess of beta hydroxybutyric and acetoacetic acid (products of disturbed metabolism of fats known as ketone bodies; formed in the liver). These acids combine with the base of bicarbonate to form salts that are excreted in the urine. The bicarbonate of the blood is thus reduced. At the same time the output of urine is increased because of the increased amount of material to be eliminated. (Ammonia excretion is also increased.) In addition there is dyspnea which actually amounts to air hunger, due to acidotic stimulation of the respiratory center. Thus, great amounts of fluid are lost by the kidneys, the lungs, and the skin (through diuresis, labored breathing, and sweating) and the result is dehydration.

In intestinal obstruction the loss of gastric hydrochloric acid by excessive vomiting lowers the blood chloride (hypochloremia); carbon dioxide is retained to compensate for the lost chloride and there results an increase in plasma bicarbonate. The excess of base constitutes an alkalosis. If the blood becomes definitely alkaline (pH, 7.6), tetany may occur. (See Chapters 12 and 20.) Nature attempts to counteract an alkalosis by an increased excretion of fixed base in the urine (which becomes alkaline and shows a decrease in ammonia content); breathing is depressed (in order to retain carbon dioxide) and the alveolar CO_2 ten-

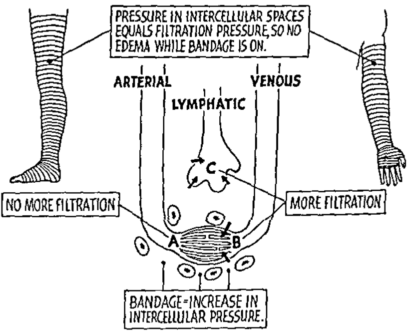

FIG. 99.—Diagram illustrating the effect of bandage treatment on edema in the extremities. A compression elastic bandage is tightly applied, as shown, *for ten minutes*; it is then removed and the extremity is massaged. This is repeated at frequent intervals. The bandage raises intercellular pressure and also intracapillary hydrostatic pressure until the two are equal. This precludes filtration of fluid by hydrostatic forces, but the osmotic pull of the blood absorbs water, and, if the lymphatics are unobstructed, *proteins are absorbed as well. Since lymph is propelled by* external compression (due normally to muscular contraction, motion, and arterial pulsation), the intermittent method of pressure *is superior to continuous pressure in lymphatic stasis.* Because of the increased intravenous pressure due to bandage (which must be less than systolic pressure) new collaterals will form and thereby improve *the venous return.* Edema due to thrombophlebitis may be helped by the injection of procaine into the sympathetics (paralyzing the vasoconstrictors) or more easily by the use of *local* heat. *This relaxes the spasm* of the veins involved and also the arteries, decreasing intravenous pressure and increasing arterial inflow, thereby reducing the stagnant anoxia and *capillary* leakage. *Elevation of the part* empties the veins, decreases hydrostatic pressure, and aids in the treatment of postphlebitic, but not lymphatic, edema.

sion is increased. More water is needed to accomplish the excretion of the excess base, and since there is less sodium, less water remains in the tissues for osmotic reasons and dehydration results.

In severe diarrheas pancreatic juice with much base is lost; consequently plasma bicarbonate is reduced (acidosis), and acid radicals are excreted in the urine. Great amounts of water are thus lost through the diarrhea and the water used by the kidneys. The loss of base in such conditions is a primary cause of dehydration. Later there is impaired renal function and more loss of base.

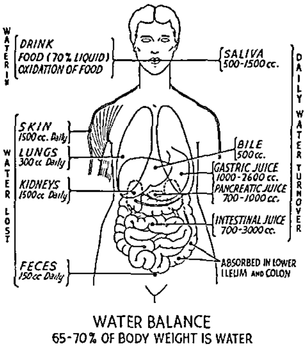

Fig. 100.—Diagram illustrating the water balance of the body. Water is obtained from liquids, food, and the oxidation of food. It is lost through the skin, lungs, kidneys, and feces. About four gallons of water are secreted by various glands and absorbed in the lower ileum and colon.

In most conditions in which there is dehydration there is also a loss of protein which occurs due to increased capillary permeability (infections, stagnant anoxemia, anoxic anoxemia when great distention of the bowel occurs), trauma to tissue at operation, as well as diminished supply due to starvation or liver damage. Therefore, it is well to consider *abnormalities in protein in relation to the amount of water and electrolytes.*

Hyperproteinemia and Its Relation to Dehydration.—In dehydration there is an increase in serum proteins, chiefly globulin. Should it continue, stagnant anoxemia develops, capillaries lose *protein*, and dehydration shock follows. The rapid concentration of blood, whether it occurs from loss of whole plasma (burns, trauma) or the protein fraction (plasmapheresis), or the aqueous fraction, leads to deficient oxy-

genation. This results in dilatation and an increase in the number of functioning capillaries so that an increased diffusion of oxygen can occur. The increased dilation and permeability is due to the local effect of poorly oxygenated blood. Pulmonary capillaries are also congested leading to pulmonary edema with more anoxia.

Hyperproteinemia is almost always due to an increase in serum globulin except in hepatic disease, acute glomerulonephritis, and where there is a simultaneous occurrence of two conditions—one causing hyperglobulinemia, the other hypoalbuminemia. Hyperglobulinemia is said to exist if the serum globulin is above 3 Gm. per 100 c.c. This is usually due to chronic infections, such as syphilis, lymphopathia venereum, and tuberculosis. Serum proteins above 9 Gm. are rarely found except in multiple

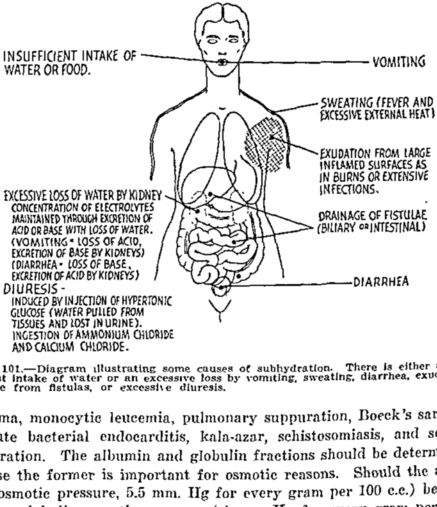

Fig 101.—Diagram illustrating some causes of subhydration. There is either an insufficient intake of water or an excessive loss by vomiting, sweating, diarrhea, exudation, drainage from fistulas, or excessive diuresis.

myeloma, monocytic leucemia, pulmonary suppuration, Boeck's sarcoid, subacute bacterial endocarditis, kala-azar, schistosomiasis, and severe dehydration. The albumin and globulin fractions should be determined because the former is important for osmotic reasons. Should the albumin (osmotic pressure, 5.5 mm. Hg for every gram per 100 c.c.) be low and the globulin osmotic pressure (.4 mm. Hg for every gram per 100 c.c.) be high, anuria and edema may result even though the total protein is normal or above.

Hypoproteinemia and Its Relation to Dehydration.—When plasma proteins are reduced, serious changes may occur. Since most of the plasma protein is synthesized in the liver it is well to classify hypo-

proteinemia under three heads: (1) Prehepatic. There is interference with intake, digestion, or absorption. The liver is normal but the supply is deficient. (2) Hepatic. There is a normal supply but the liver is unable to build protein. (3) Posthepatic. There is an abnormal loss of protein. Since a loss of 1 Gm. of serum albumin means a loss of 30 Gm. of tissue protein, the term protein deficiency may be more appropriate because it is not only blood proteins that become deficient but tissue protein as well. When hypoproteinemia exists, only 3 per cent of ingested nitrogen is fabricated into plasma proteins; the remainder is used to replenish tissue protein. Therefore, in evaluating hypoproteinemia, more than one determination must be made to know the protein reserves.

The causes or pathogenesis of hypoproteinemia are as given in Table X.

TABLE X

I PREHEPATIC	II HEPATIC	III POSTHEPATIC
(a) Nutritional—starvation or malnutrition	(a) Acute yellow atrophy of liver (b) Thyrotoxicosis (c) *Hepatic disease from any cause*	(a) Hemorrhage (b) Shock (c) Burns (d) *Nephrosis* (e) Excessive loss of nitrogen as in thyrotoxicosis and anesthesia (f) Peritonitis

Postoperative hypoproteinemia may be due to all three types; moreover, any type soon involves the others, for a low plasma protein from any cause soon produces liver dysfunction and the reverse is true. The effects of diminished protein are seen clinically in the following:

(1) Shock, which may be due to loss of plasma, loss of nitrogen in urine, decreased ingestion of protein, and inability of liver to synthesize protein.

(2) Suppression of urine due to low osmotic pressure. No fluid is drawn into blood from the tissue spaces where fluid accumulates.

(3) *Hemoconcentration.*

(4) Abdominal distention due to edema of bowel wall and hypomotility. The distention also may be causative due to anoxia caused by interference with respiration and local venous stasis or inflammation. Subcutaneous edema is not always present in edema of the bowel because of the local factors and looseness of tissue in the gastrointestinal tract.

(5) Edema. There is no special level at which this occurs. It varies greatly and is influenced by muscular action, gravity, tissue pressure and venous pressure, hydration (edema would be delayed in dehydration even with low protein), salt and fluid intake, kidney function, and bowel function (diarrhea or vomiting). Usually the edema is peripheral first; then it occurs in the gastrointestinal tract and lungs.

(6) Ascites due to portal obstruction but also hypoalbuminemia (hepatic type). Hydrothorax and hydropericardium.

(7) Delayed and deficient wound healing due to decreased fibroplasia and edema.

(8) Resistance to infection is lowered.

(9) Postoperative asthenia.

(10) Restlessness and irritability.

(11) Decubitus and skin ulcers, also peptic ulcer, which may result from rigid diet with low protein and be improved by high protein diet.

Diagnosis of Hypoproteinemia.—The diagnosis is made by measuring plasma proteins. Several precautions should be taken. In dehydration protein levels may be high yet the total amount of circulating protein low. Total protein may be normal but albumin low. Therefore, a hematocrit should be done and also albumin-globulin determinations. Thus a dehydrated patient may show normal amount of protein. After sufficient fluid physiological saline is given to overcome dehydration, the value of protein goes down and edema may result which is due to hypoproteinemia and not the salt solution.

A hypoproteinemia may exist with normal protein levels in dehydration and there may be no lowering of blood chloride values or elevation of hematocrit, especially if there is a severe anemia. Also there may be a low total volume of protein with plasma protein and blood in normal relations. Blood volume determinations are usually made with T-1824 or Evans' blue dye, and available fluid determinations are made by the sodium-thiocyanate method. In dehydration if the fluid lost has the same electrolyte pattern quantitatively and osmotically as plasma, then the concentration of Na and Cl in the plasma may be normal when the body needs NaCl. Hepatic bile and fluid from the intestinal mucosa contain approximately the same amount of fixed base and chloride as does plasma. Loss of this fluid will cause a reduction of the volume of blood plasma and of interstitial fluid but should not alter the plasma chloride (or bicarbonate) concentrations.

The Prevention and Treatment of Hypoproteinemia.—The average man requires about 3,000 calories a day divided as follows:

Carbohydrate	400 Gm. × 4.1 calories per gram	1640 calories	53%
Fat	115 Gm. × 9.3 calories per gram	1070 calories	35%
Protein	90 Gm. × 4.1 calories per gram	369 calories	12%
		3079 calories	100%

For acute or chronic protein deficiencies, protein should be given by mouth if at all possible. These may be given as concentrates or hydrolysates. Twenty-five per cent of the calories should come from protein, not over 15 per cent from fat, and 60 per cent from carbohydrate. A diet of 150 Gm. of protein a day may be given orally as follows: milk (skimmed), cottage cheese, lean meats including liver and pancreas, egg albumin, soybean. In addition, oral vitamins should be given:

vitamin A, 1,500 units; vitamin D, 1,500 units; ascorbic acid, 225 mg.; thiamine, 9 mg.; riboflavin, 6 mg.; nicotinic acid, 60 mg.

In acute conditions, blood, plasma, and albumin should be given intravenously in combinations to restore blood volume, red blood cell volume, plasma volume, and plasma protein levels to a point where the circulation is adequate. Serum albumin is available in amounts of 25 Gm. This is osmotically equivalent to approximately 500 c.c. of citrated plasma; it is dissolved in 100 c.c. of buffered diluent, giving a 25 per cent solution. It is not often used because it is very expensive and not readily available. If dehydration is present in addition to shock, it is perhaps unwise to use a concentrated solution which must depend on interstitial fluid to restore isotonicity. Since interstitial fluid is depleted, shock and dehydration may be increased. Acid hydrolysate of casein (Parenamine) or enzymatic hydrolysate of casein and pancreas (Amigen) with glucose may be given by vein in *less acute* deficiencies where liver function is normal. However, its use intravenously loses the selective action of the intestine and its utilization is doubtful. A 5 per cent solution of casein hydrolysate in 5 per cent glucose may be used in pre- and post-*hepatic types. Only one-half of the nitrogen in aminoacids is utilized.* The rest is deaminized and used as a source of calories. This mixture is about 25 per cent protein (metabolically) and 75 per cent carbohydrate; that is, in 1,000 c.c. there will be 25 Gm. protein and 50 Gm. carbohydrate. This solution should be given slowly, about 500 c.c. of a 5 per cent solution per hour. But even if given in this way, utilization is doubtful and reactions occur.

Plasma can be used *in chronic deficiencies. However, since* for every gram of plasma protein 30 Gm. of tissue protein are lost or gained, a patient needing 200 Gm. of protein would require 30,000 c.c. of plasma; that is, 7 Gm. per 100 c.c. It is better to use hydrolyzed proteins by mouth. Ascitic fluid and pure amino acids have also been employed. Reactions do occur, with fever, nausea, and thrombosis of the vein in any of the plasma substitutes. Posthepatic types of deficiencies are more *successfully treated than hepatic types. In the hepatic types* plasma substitutes are probably not synthesized. Vitamins may be given intramuscularly: vitamin C, 500 mg.; thiamine, 20 to 40 mg.; riboflavin, 20 to 40 mg.; niacin, 150 mg.

In restoring plasma and blood in acute deficiencies they may be given as fast as the circulation will take them. One thousand cubic centimeters should be given to begin with. The laboratory helps to evaluate the amount needed (hematocrit and plasmaprotein). The best guide, however, is the urine output in amount and specific gravity (if kidneys are normal) which should range from 1.010 to 1.023; also there should be normal body temperature, improved sensorium, slower respiration, increase in blood pressure, slowing of pulse, and sweating.

As a general rule, when capillaries are normal in size and permeability, crystalloids are useful; when dilated and permeable blood and

plasma should be used. In such conditions as severe septicemias where hematocrit and plasma proteins are apt to be low, recovery is helped by transfusions of whole blood and plasma. With widely dilated capillaries these infusions leak out especially the plasma. If by laboratory tests they are found to remain in the blood stream, a better prognosis may be given.

SYMPTOMS OF DEHYDRATION.—Unless ample fluid is given in the acute *water deficiency states*, symptoms of dehydration soon occur. We shall learn in Chapter 13 that with proper treatment the patient may lose up to 40 per cent of the blood volume and recover. However, serious symptoms result if only 10 per cent of the water is lost. This amounts to about 6 per cent of the body weight.

The effects of dehydration are (1) a loss in body weight with great weakness; (2) acidosis causing dyspnea and drowsiness (due to anhydremia which depresses oxidation and causes an accumulation of lactic acid in the tissues); (3) decreased urinary output and in severe degrees with shock, anuria (this also tends to cause acidosis through retention of phosphoric and other acids); (4) increase in nonprotein nitrogen of the blood (insufficient water for kidney excretion, (5) rise in temperature due to decrease in circulating fluid and insufficient fluid for vaporization, also causing anorexia and malaise; (6) thirst, due to insufficient water for salivary gland action and consequently dry mouth, tongue, and throat; (7) dry skin and sunken eyes, due to loss of subcutaneous fluids; the hematocrit reading is elevated, the concentration of plasma protein is greatly increased, and the blood is thick (hemoconcentration); (8) drainage from fistulas (such as drainage from the common duct following choledochostomy) will be greatly reduced. (9) The McClure-Aldrich test will show a shortened absorption time.

DIAGNOSES OF DEGREES OF DEHYDRATION.—Many clinical and laboratory tests *help us to diagnose which factor is at fault.* Vomiting and diarrhea are self-evident, as is also the loss of fluid in proteins from fistulas or large exudating surfaces, as in burns or extensive infections. The quantity of urine and its specific gravity give good evidence of dehydration. Estimations of the total amount and proportions of the plasma protein will often show the cause of the edema. The character of the edematous fluid will also show the nature of the edema: if this fluid is high in protein content, it indicates a plasma edema; if low in protein, a lymphedema. The diagnosis may also be aided by a quantitative estimation of the blood chlorides and the chloride excreted in the urine. Determination of the carbon dioxide combining power will reveal a state of acidosis or alkalosis. Knowing the amount of blood chlorides and the CO_2 combining power, one may estimate the amount of sodium ions in excess of chloride ions, thereby avoiding the time-consuming task of sodium determination. However, the amount of sodium potassium or other cations may be quickly determined by the use of the

Beckman flame spectrophotometer. An increase of potassium in the urine may mean loss of intracellular fluid, and in addition to its indication of cell damage, the potassium itself may be toxic and may be a *factor in the production of shock. The hematocrit* will differentiate between hemorrhage and shock. In hemorrhage there will be a high plasma-low cell ratio; in shock there will be a low plasma-high cell value. Also the size of the cells are indicators of volume of intracellular water; *that is, the mean corpuscular volume. Studies in sodium and potassium* are important because the former is the chief cation of intercellular fluid and the latter is the chief cation of intracellular fluid. The red corpuscle count, hematocrit, and hemoglobin as well as specific gravity of blood and plasma proteins are increased *in dehydration (except in anemia). The* relationship of these factors to each other is constant here.

The McClure-Aldrich test (see Chapter 4) is thought to reveal an impending state of subhydration before symptoms are present. This is due to slight hemoconcentration, which in turn causes a withdrawal of fluid from the intercellular spaces, increasing their avidity for water. This test is not entirely reliable.

The Prevention and Treatment of Dehydration.—We have already noted how the plasma proteins are closely associated with the normal and abnormal movement of water. We have also considered the relationship between water and electrolytes. Let us now review the body's needs for water and the correction of abnormal amounts of water loss.

We have seen that the normal man needs about 5 Gm. of salt a day and in extreme conditions as many as 15 Gm. He also needs approximately 90 Gm. of protein and 400 Gm. of carbohydrate. Fat is not necessary because it is available in the tissues. He also needs about 3,500 c.c. of water a day—2,000 c.c. for vaporization and 1,500 c.c. for the urine. Infants require 2½ to 3 ounces per pound per twenty-four hours. Since the skin, lungs, and gastrointestinal tract take the available interstitial water first, the kidneys may be looked upon as buffer organs working with whatever amounts are left over. With normal kidneys water is easily disposed of and therefore more water may be given safely.

If the patient is losing large amounts of fluid by vomiting, diarrhea, biliary fistula, etc., large quantities of fluid may be necessary. In such conditions one is guided by the amount lost (if this can be estimated), by the urinary output, and by the clinical symptoms and signs of dehydration as well as the laboratory aids.

The clinical signs to watch are: (1) Body temperature and skin—if the temperature is normal and the skin moist, there is enough water for the regulation of vaporization. (2) Amount of urine and its specific gravity and reaction—if normal, this means enough fluid is available for the "buffer" organ and if not too concentrated (over 1025) the tubules have conserved a normal amount of water. (3) Pulse and blood pressure—a rising pulse with fall in blood pressure means a reduced circu-

lating blood volume. (4) *Respiration—if rapid means stagnant anoxemia.* (5) Sensorium—if dull means dehydration and perhaps cerebral anoxia. (6) Edema—with bedfast patients this is often observed first *in the flanks and posterior axilla;* if the patient is sitting up, ankle edema. Many writers contend that one should not wait for edema to prove hypoproteinemia. This is not intended to supplant laboratory tests. However, it is true that laboratory aids frequently reveal normal values when edema is present. If the patient has not received too much sodium (hypernatremia) the presence of edema means hypoproteinemia regardless of tests. The reasons for this have been discussed previously. (7) Thirst is unreliable as a guide because with severe depletion of sodium (as in vomiting) there may be no thirst or oliguria. In starvation thirst is extreme and oliguria is present. (8) Color of face and lips (dusky red) and dry mouth are present in severe dehydration.

Laboratory aids need not be extensive: erythrocyte count, hemoglobin, plasma proteins with albumin, globulin fractions, and hematocrit; occasionally the CO_2 combining power and blood chlorides. The latter shows the amount of sodium ions in excess of chlorine ions and eliminates the necessity for sodium determination. A very useful test to evaluate salt depletion is the urine chloride test (Fantus). It is done as follows:

Urine Chloride Concentration Bedside Test

Materials used

1. Clean test tubes
2. Medicine dropper (standard size)
3. 20 per cent potassium chromate
4. 2.9 per cent silver nitrate
5. Distilled water for rinsing

Technique

10 drops of urine in test tube plus one drop 20 per cent potassium chromate. Then add drops of silver nitrate, drop at a time, shaking until yellow color turns brick red (end point).

Number of drops of silver nitrate equals urine sodium chloride concentration in grams per liter (3 grams per liter per twenty-four hours normal). *Urinary output per twenty-four hours should be about 1,500 c.c.*

Azotemia is a secondary effect and it indicates kidney damage. Therefore, a nonprotein nitrogen determination is indicated.

Methods of Replacing Fluids.—The best method of replacing fluids is by mouth. Where no contraindication is present, such as edema due to low protein or burn shock (see Chapters 6 and 14), thirst is a good indicator of the amount required, and water may be given as desired over and above the minimum requirement.

It is well to remember that water and glucose are absorbed not in the stomach but in the small intestine.

The type of fluid may have to be regulated. Workers in extremely hot temperatures lose chlorides through sweating and will have heat

exhaustion unless they are given sufficient salt with their drinking water. Patients with nephrosis lose so much protein through the kidneys that a high protein diet must accompany liberal amounts of water.

Should a patient be unable to take fluids by mouth, intravenous therapy is best. However, hypodermoclysis is very effective and is particularly useful in those in whom intravenous therapy is difficult (newborn, patients with poor veins, obese patients), in those in whom a sudden increase in blood volume is undesirable (cardiac disease), and in patients whose osmotic equilibrium is difficult to maintain (burns, fistulae in children). *Physiological saline is the safest solution to use. If rapid* absorption is desired, lyophilized hyaluronidase (Hydose—Wyeth) may be added. It is said to liquefy the hyaluronic acid gel present in connective tissues which normally act as a barrier to diffusion. In the average adult 1,000 c.c. are injected (slowly) every 8 hours. Physiological saline is the most useful but may produce so-called salt block if used in excess. Even vomiting causes a loss of only about 5 Gm. of salt per liter. Physiological saline contains about 9 Gm. per liter. Perhaps the best solution to use with saline is 5 per cent glucose in distilled water. This is isotonic and will supply sufficient carbohydrate fuel to prevent acidosis. In cases of intestinal obstruction it is well to alternate or vary the two solutions as required.

Even if water (without salt or glucose) could be absorbed, it would be eliminated by the kidneys without benefit to the body. For example, in intestinal obstruction gastric juice, with its chloride, is lost due to vomiting. Much base is left, which is excreted by the kidneys, with the result that sodium and chloride are depleted in the extracellular fluid. Therefore the need for sodium chloride, and because of local factors and anoxemia a loss of protein occurs which must be corrected.

A study of the blood chlorides and the carbon dioxide combining power aids in the proper evaluation of a possible alkalosis (treated by giving chloride) and acidosis (treated by giving bicarbonate). Ringer's solution or lactated Ringer's solution (Hartmann) is used in dehydration due to diarrhea. In every instance intravenous fluids must be supplemented by blood or plasma transfusion to keep up the normal osmotic index. In severe dehydration potassium as well as sodium must be supplied.

The most practical way to determine the need for transfusion is to evaluate the degree of hemoconcentration. This may be done by determining the hematocrit, the serum proteins, the number of red blood cells, and the hemoglobin.

Types of Solutions Used for Intravenous Therapy in Dehydration.—Physiological saline is .85 per cent. The word "*normal*" saline is frequently used. This is technically not correct. Normal saline is 5.846 per cent. A normal solution contains 1 Gm. equivalent of a particular constituent of the solute in a liter of solution. Equivalent weight is the atomic weight divided by the valence (see Chapter 12). A normal solu-

tion of NaCl = 58.46 Gm. per liter. Physiological or isotonic saline contains 10 per cent more sodium and 50 per cent more chloride than does plasma. The excess chloride is eliminated through the kidneys (if functioning), leaving sodium to combine with bicarbonate. This prevents or alleviates acidosis.

Glucose solutions of 5 per cent are isotonic. Glucose is not an electrolyte and therefore does not dissociate into ions. Sodium chloride does dissociate and exerts a much greater osmotic pressure because each molecule of an electrolyte is split into 2 parts (ions) and each of these exerts its separate pressure effect. Therefore saline has twice as many active particles even though the number of molecules is the same. Dextrose is especially indicated in ketosis.

Sodium racemic lactate. One-sixth molar sodium lactate is isotonic (1 part molar sodium lactate to 5 parts distilled H_2O). Lactate requirements may be calculated if the bicarbonate level in the blood is known. Ten cubic centimeters of solution per kilogram of body weight are required to raise the carbon dioxide content of the blood 10 volumes per cent (Talbott). This solution is useful in acidotic states.

Ringer's solution is useful in diarrheas of children because it contains sodium, calcium, and potassium.

Hypotonic solutions, 0.45 per cent of NaCl or 0.38 per cent NaCl plus 0.11 per cent $NaHCO_3$, are advocated by Coller in postoperative dehydration.

Hypertonic solutions. Glucose, sucrose, salt, or plasma may be used. Dehydration is a definite contraindication to their use because they tend to pull interstitial fluid into the blood stream. *Since interstitial fluid is already depleted, intracellular fluid is moved,* causing damage to tissue cells. Other objections to their use are: thrombosis of veins at site of injection, transient kidney damage, spasm of the duodenum, and sphincter of Oddi. If capillaries are very permeable, the solution may enter tissue spaces damaging cells.

Miscellaneous Data Concerning Intravenous Therapy: In dehydrated patients intravenous fluids cause a prompt rise in cardiac output due chiefly to stroke volume. This is not true of normal subjects.

In cardiac disease the danger of intravenous therapy is not so much the increase in blood volume as in altering the already disturbed chemistry of body fluids, further increasing osmotic derangement. *If fluids are needed, they should be used judiciously.*

There is very little elevation of venous pressure (11 cm. of water) in normal subjects even when 168 c.c. of saline are given intravenously per minute up to 2,000 c.c. There is no increase in heart rate. The peripheral and pulmonary veins and capillaries dilate to *accommodate* the fluid. *If there has been previous hemorrhage or dehydration, there is no rise in venous pressure.*

A good rule to follow: Use intravenous saline cautiously in the presence of alkalosis, hypoproteinemia, anemia, or oliguria. If in doubt,

give isotonic saline by hypodermoclysis; then, if osmotic pressure is at the edema level, the solution will remain under the skin unless given rapidly under excessive pressure (that is, over 35 mm. of mercury). Potassium citrate or chloride may be necessary rather than sodium chloride when there is alkalosis and hypokalemia and hypochloremia.

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Chapter 12
ACID-BASE BALANCE

When certain chemical substances are dissolved in water they dissociate into *ions*. These dissociated (ionized) molecules and the undissociated (un-ionized) molecules establish an *equilibrium*. Substances whose molecules dissociate are known as *electrolytes*. Ions which are positively charged are called *cations* (indicated by + sign) and those negatively charged, *anions* (indicated by − sign).

The anode is the positive pole, the cathode is the negative electrode or pole of an electric circle. When a chemical is dissociated, the ions which are given off at the positive pole, although called anions, are negatively charged (−) while those given off at the negative are called cations and are positively charged (+).

Water itself dissociates (slightly) into H^+, which is positive, and OH^-, which is negative. The law of mass action applies in each case. Simply stated, it means that *chemical equilibrium* will be established between the H^+ ions (acid) and the OH^- (alkaline). Water is neutral. When an acid is made with water as a vehicle, no matter how great the preponderance of H^+, there will always be some OH^- present. It is this degree of H^+ concentration over OH^- that determines the alkalinity; if neither predominates, there is neutrality. Thus we see that neutrality does not mean the absence of acid and alkali but enough of each to counterbalance the other. The symbol pH is used by chemists to denote the degree of acidity. When 1 mol of H ion is present in a liter of water, the pH is 0.0.

The logarithm of 1 is zero. The logarithm of 10 is 1 or unity. Any number between 10 and 100 has a common log which lies between 1 and 2, etc.

If a solution contains only 0.1 (or 10^{-1}) mol of H^+, there is less of H^+ and more OH^-; the pH is 1.0 (or the negative logarithm of 0.1). A *less* acid solution thus has a higher pH; a *more* acid solution, a *lower* pH. The relation between pH and the concentrations of hydrogen and hydroxyl ions may be seen in Table XI.

In speaking of solutions and their composition it is necessary to use a term which will serve as a common denominator to express osmotic pressure of the solution. For this reason milliequivalent is employed. This makes it unnecessary to speak in terms of grams, milligrams, and volumes per cent, because regardless of its nature, each milliequivalent has the same osmotic pressure effect. In ionized solution each ion exerts its own milliequivalent. One gram molecule is the molecular weight expressed in grams. The gram molecular weight divided by the valence of the active gram is the gram equivalent weight. Thus sodium = 23 plus

chloride = 35.46. Therefore, the gram molecular weight of sodium chloride is 58.46. The value of the active group is one. Therefore, the number remains the same. That is, the gram weight in this case is equal to the gram molecular weight.

An equivalent weight may be defined as the quotient of the atomic weight of an element divided by its valence or its change in oxidation state. The following is the formula for obtaining the equivalent weight:

$$\frac{\text{Atomic weight}}{\text{Valence}} = \text{Equivalent weight}$$

A normal solution is one that contains one gram equivalent weight per liter. A milliequivalent is 1/1000 of a gram equivalent. A mol is a gram molecule. In a solution it is the molecular weight of the active chemical expressed in grams. A molecular solution is one containing one gram molecular weight per 1,000 c.c. Chemicals act mol for mol or equivalent for equivalent. Therefore, one equivalent is equal to one equivalent and one milliequivalent is equal to one milliequivalent.

The following formula may be used to find milliequivalents per liter:

$$\text{Milliequivalents per liter} = \frac{\text{Milligrams per liter} \times \text{valence}}{\text{Atomic weight}}$$

Examples: Normally there are about 10 mg. of calcium per 100 c.c. of serum. Calcium has an atomic weight of 40.08. Its valence is 2. Thus:

$$\frac{100 \times 2}{40} = 5 \text{ meq.}$$

Potassium is present in the amount of 20 mg. per 100 c.c.; it has an atomic weight of 39.096 (roughly 40). Its valence is 1. The formula is:

$$\frac{200 \times 1}{40} = 5 \text{ meq.}$$

The following is a list of some of the more common milliequivalents. Normal values for electrolytes of human serum and plasma:

BASE—CATIONS			ACID—ANIONS		
Na^+	136-145	meq. per liter	HCO_3^- (vol. % CO_2)	26-28	meq. per liter
K^+	3.5-5.0	meq. per liter	Cl^-	98-106	meq. per liter
Ca^{++}	4.5-5.0	meq. per liter	HPO_4^-	2-3	meq. per liter
Mg^{++}	2-3	meq. per liter	SO_4^-	1.0-1.5	meq. per liter
			Organic acid	5-7	meq. per liter
			Protein	14-19.5	meq. per liter
Total	146-158.0	meq. per liter	Total	146-158	meq. per liter

The following is a list of the inorganic ions and the method of conversion from milligrams per 100 c.c. to milliequivalents:

$Na^{\cdot}$	mg. per 100 c.c. × 10 ÷ 23	HPO_4''	(mg. P) per 100 c.c. × 10 ÷ 31 × 1.8
$K^{\cdot}$	mg. per 100 c.c. × 10 ÷ 39	SO_4''	(mg. S) per 100 c.c. × 10 ÷ 32 × 2
$Ca^{\cdot\cdot}$	mg. per 100 c.c. × 10 ÷ 40 × 2	$H.HCO_3$ and $BHCO_3$	vol. % ÷ 2.22
$Mg^{\cdot\cdot}$	mg. per 100 c.c. × 10 ÷ 24 × 2	Protein	(Gm. per 100 c.c.) × 2.43
Cl'	mg. per 100 c.c. × 10 ÷ 35		

The valency of HPO_4 is taken as 1.8 because, at the normal pH of extracellular fluid, 20 per cent of the concentration of this radical carries one equivalent of base (BH_2PO_4) and 80 per cent two equivalents (B_2HPO_4), B representing univalent base. Base equivalence per unit of (HPO_4) is therefore 0.2 + (0.8 × 2) = 1.8. The double valency sign is to this small extent inaccurate. For all practical purposes, however, the valency is given as 2 instead of 1.8.

Hydrogen Ion Concentration

The reaction of a solution expressed in terms of hydrogen ion concentration may be expressed positively. However, the quantities involved are so small that this would

necessitate using complicated fractions. For example, the hydrogen ion concentration of normal sodium hydroxide amounts to 0.00000000000001. This value may also be expressed as 1×10^{-14}. The symbol $^{-14}$ to the right of the figure 10 is termed the exponent, or index, and means that in order to express the value in the form of a decimal fraction, the figure 1 must be placed 14 places to the right of the decimal point. Another way to express the fraction would be 1/100000000000000. Other examples of this method of expression: 10^{-1} means 0.1 or 1/10; 10^{-2} means 0.01 or 1/100; 10^{-3} means 0.001 or 1/1000, and so on. (Best and Taylor).

In 1909 Sorensen introduced a system of notation by which the common logarithm (that is, the logarithm to the base 10) of the decimal fraction expression the H ion concentration is employed as a positive number. For example, the H ion concentration of serum is 0.0000004 normal. This could be expressed either as 4×10^{-8}N or as $1 \times 10^{-7.4}$N. The latter expression is simplified by omitting the 10 and replacing the minus sign of the exponent by the symbol pH (hydrogen ion exponent). This gives the value as 7.40 which is derived as follows: The log of the figure 4×10^{-8} is 0.6021 which is subtracted from the negative exponent 8, or − 7.40. The minus sign is then omitted.

TABLE XI

THE RELATION OF PH TO THE CONCENTRATION OF HYDROGEN AND HYDROXYL IONS IN A SOLUTION

	pH	mols per L. [H +]	[OH −] mols per L.
	14.0	0.00000000000001	1.0
	13.0	0.0000000000001	0.1
ALKALINITY	12.0	0.000000000001	0.01
	11.0	0.00000000001	0.001
	10.0	0.0000000001	0.0001
	9.0	0.000000001	0.00001
	8.0	0.00000001	0.000001
NEUTRALITY→	7.0	0.0000001	0.0000001
	6.0	0.000001	0.00000001
	5.0	0.00001	0.000000001
ACIDITY	4.0	0.0001	0.0000000001
	3.0	0.001	0.00000000001
	2.0	0.01	0.000000000001
	1.0	0.1	0.0000000000001
	0.0	1.0	0.00000000000001

It is not necessary for practical purposes to be able to compute these values. It is, however, well to remember that since the figures are logarithmic, a *very small number indicates a great change.* A change of 1 unit is a tenfold change; 0.3 change is a doubling or halving (depending upon which direction); 0.1 is 4/5 or 5/4 (a pH of 4.1, for instance, is 4/5 as acid as a pH of 4.0; and a pH of 4.0 is 5/4 more acid than a pH of 4.1).

By consulting Table XI it will be seen that the figures though stated positively are really negative values; therefore, the greater the number, the less acidity.

"The greater the degree of dissociation of acid, the greater will be the H ion concentration and the greater consequently will be its acid nature. Thus HCl, though it contains only one atom of hydrogen in its molecule, undergoes almost complete dissociation and is a stronger acid than H_2CO_3, which has two hydrogen atoms but dissociates to a small extent." (Best and Taylor.) As the H^+ concentration is lowered, the logarithmic figure increases, until at pH 7.0 the solution is neutral, and when the pH is more than 7.0 the solution is alkaline. Since the figures refer to powers of 10, a pH of 5.00 is 10 times more acid than a pH of

6.00, etc. A pH of 11.00 is 1,000 times more alkaline than a pH of 8.00 (that is, the change equals $10^3 = 10 \times 10 \times 10 = 1{,}000$), etc.

The blood is normally slightly alkaline and remains at about pH 7.4 regardless of the fact that acids (phosphoric, sulfuric, hydrochloric, carbonic, and lactic) are continually entering it. Nature guards this pH as rigorously as the osmotic index or the body temperature. This stability is a part of what Cannon terms homeostasis and is in no small measure related to the action of the sympathetic nervous system. This constant pH is maintained through the action of (1) buffer systems of the blood (substances which take up acids or alkalis), (2) excretion of carbon dioxide by the lungs, and (3) excretion of fixed acids or bases by the kidneys.

Buffer systems of the blood are found (Best and Taylor):

I. In the plasma as
   (1) Free acid (carbonic), and acid bound as sodium bicarbonate; that is, the salt of that acid
   (2) Acid and alkaline phosphates of sodium
   (3) Plasma proteins (which behave as acids and combine with base)

II. In the corpuscles (secondary buffers)
   (1) Oxyhemoglobin and reduced hemoglobin (acid) and potassium salt of pigment (alkaline)
   (2) Potassium salts (acid and alkaline) of phosphoric acid

The excretion of carbon dioxide by the lungs and the absorption of oxygen by the blood is accompanied by a chloride bicarbonate shift.

The absorption of oxygen from the alveolar air is the result of diffusion; that is, there is a greater pressure of O_2 in the alveoli of the lung than in the arterial blood. This difference in partial pressures causes oxygen to pass from the alveoli into the plasma in simple solution and then into the red blood cells. The hemoglobin in the blood leaving the lungs is about 95 per cent saturated in the form of oxyhemoglobin. Practically no oxygen is lost from the arterial blood until it reaches the capillaries. The oxygen tension of tissue fluids and cells is low. Therefore oxygen flows from plasma through the capillary wall to the cells. The plasma oxygen tension is thus lowered and oxygen is released from the red blood cells to the plasma. The reverse is true in the tissues where CO_2 tension is higher than in the blood plasma. Accordingly CO_2 enters the plasma. Here it combines with water to form carbonic acid, $H_2O + CO_2 = H_2CO_3$. This is formed in the red blood cells and not the plasma because the former contains a catalytic enzyme, carbonic anhydrase, which starts the process. At the same time oxyhemoglobin becomes reduced. Reduced hemoglobin is a weaker acid than oxyhemoglobin and therefore it gives up its base to the carbonic acid. Most of the base comes from hemoglobin directly or indirectly. Thus potassium bicarbonate and acid hemoglobin are formed.

$$H_2CO_3 + KHb \longrightarrow HHb + KHCO_3.$$

This reaction causes a higher concentration of bicarbonate ions (HCO_3^-) in the cells than in the plasma and therefore two-thirds of these ions or more diffuse out of the corpuscle. The corpuscle membranes are impermeable to the cations calcium, sodium, and potassium as well as the colloidal anions hemoglobin and plasma proteins. Therefore ionic equilibrium between plasma and cell will be disturbed. To adjust this, Cl^- ions diffuse from the plasma into the corpuscles. The HCO_3^- ions which leave the cells combine with the sodium released from chloride to form plasma bicarbonate, and, as we have seen, the chloride ions combine with potassium within the cells. It is the bicar-

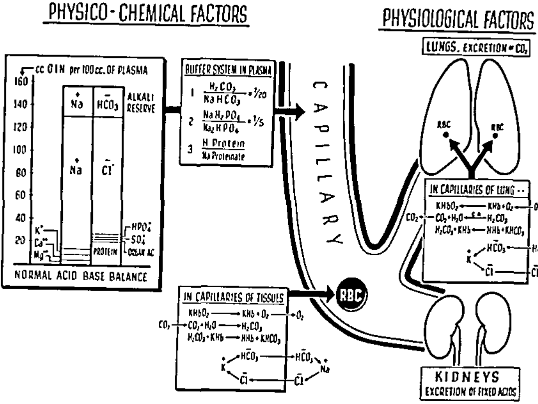

Fig. 102.—Diagram illustrating the maintenance of the pH of the blood. The pH is maintained by physicochemical factors (buffer action) and by physiological factors (regulation of the amount of fixed acids excreted by the kidneys and of the amount of CO_2 eliminated by the lungs). Bicarbonate ions are formed in the erythrocytes, and most of them diffuse out into the plasma, and in return chloride ions diffuse in. Base does not pass because the erythrocytes, though permeable to anions, are impermeable to cations. This mechanism is known as the chloride shift; that is, as bicarbonate goes out, it is accompanied by a shift of chloride into the cell. As blood passes from the arterial to the venous side, carbon dioxide is absorbed and diffuses into the red cell. Some of this is explained on the basis of partial pressures of gases because as the red cell goes to the tissue spaces, it loses some of its oxygen due to the fact that the pressure of oxygen in the tissue spaces is less than that in the red cell. The reverse is true of carbon dioxide. The largest part of freshly generated carbon dioxide is carried by the red blood corpuscles. When the carbon dioxide is absorbed and diffuses into the red cell, a change occurs through the action of carbonic anhydrase, an enzyme, converting the carbon dioxide into carbonic acid (H_2CO_3). The oxyhemoglobin becomes at the same time reduced. Reduced hemoglobin is a much weaker acid than oxyhemoglobin and so gives up its alkali to the carbonic acid. Potassium bicarbonate ($KHCO_3$) and acid hemoglobin (HHb) are thereby formed. The base which previously had been bound to the nondiffusible hemoglobin is now bound as bicarbonate. The concentration of bicarbonate ions (HCO_3^-) in the cell is thereby raised above that in the plasma, and as a result this anion diffuses across the corpuscular membrane. Since the cations cannot diffuse, the ionic equilibrium between the plasma and the interior of the cell will tend to become disturbed. The balance is adjusted by the diffusion of chloride ions (Cl^-) from the plasma into the corpuscles where they combine with the base. The bicarbonate ions (HCO_3^-) which leave the cells combine with the sodium released from chloride to form plasma bicarbonate. As a result of this chemical exchange, the osmotic index within the cells is increased and water, therefore, passes from plasma into the corpuscle, and the latter increases in volume.

At the same time that this shift is going on in the tissue spaces, a similar shift in an opposite direction takes place in the lungs where CO_2 leaves the blood and hemoglobin becomes a much stronger acid as a result of oxygenation. The alkali is released from its combination with chloride and recombines with hemoglobin. The chloride passes out of the cell. The base furnished by hemoglobin thus serves as the chief means by which CO_2 is carried from the tissues to the lungs.

In the diagram this buffer action is illustrated in the tissue spaces as follows: Potassium hemoglobinate when it is reduced gives rise to potassium hemoglobin plus oxygen and oxygen goes to the tissues. At the same time CO_2 enters the red blood cell, it combines with water due to the action of carbonic anhydrase, forming carbonic acid. Carbonic acid plus potassium hemoglobin gives rise to acid hemoglobin plus potassium bicarbonate. The bicarbonate that goes out into the plasma combines with the sodium. The chloride enters the cell and combines with the potassium. In the capillaries of the lung the reverse takes place. Oxygen enters the red blood cell and combines with potassium hemoglobin to form potassium hemoglobinate. At the same time carbonic acid is reduced due to the action of carbonic anhydrase, giving rise to water plus carbon dioxide. The latter is given off. Potassium bicarbonate plus acid hemoglobin gives rise to potassium hemoglobin and carbonic acid. The shift takes place, bicarbonate goes in, chloride goes out. The rest of the buffer system is present in the plasma. The primary buffers consist of (1) carbonic acid (free acids) and acid bound as sodium bicarbonate; the ratio is 1 to 20; $\frac{HHCO_3}{BHCO_3} = \frac{1}{20} = \frac{1.35\ \text{meq./L.}}{27\ \text{meq./L.}} = \frac{3\ \text{vol. \%}}{60\ \text{vol. \%}}$; (2) acid sodium phosphate (a weak acid) and alkaline sodium phosphate (the salt of the buffer pair); ratio about 1 to 5; (3) plasma proteins which at the reaction of the blood behave as acids and so they combine with base. (Diagram showing the normal acid-base balance and chloride shift modified from Best and Taylor.)

bonate shift which makes the "chloride shift." Since blood is a liquid within a liquid, any increase in osmotically active substance within cells will cause water to enter—this occurs in the corpuscle which attracts water from plasma and thereby increases in volume.

In the lungs where CO_2 leaves the blood and hemoglobin becomes a stronger acid (oxyhemoglobin), base is released from chloride and combines with hemoglobin.

$$KHCO_3 + KHb \rightarrow KHb + H_2CO_3.$$

Chloride leaves the cell and bicarbonate enters. The base furnished by hemoglobin is as we have noted the chief means by which CO_2 is carried from tissues to lungs.

The Excretion of Fixed Acids or Bases by the Kidneys.—Normally the glomerular filtrate is neutral, the reaction of bladder urine is acid. By this transformation base is retained and acids are lost. Since the body has only a limited supply of base and cannot make it, all inorganic base lost must be ingested in food. It is therefore vital that base be conserved. Acids are the products of metabolism and are formed in large quantities; therefore they must be eliminated. The formation of ammonia from glutamine, and to a small extent from amino acids in the tubular epithelium, provides another means for the neutralization of acid allowing inorganic base to be returned to the body. When an excess of acid appears in the blood, the kidneys excrete it. If there is an excess of alkali, the kidneys will eliminate base.

A very practical exception to this rule has been reported by Van Slyke and Evans. In extreme dehydration, hypochloremia, and alkalosis the urine may be acid. They found that despite alkalosis (excess, plasma bicarbonate) the urine was pH 5 to 6.4. They attribute this phenomenon to the fact that the body deficiency of sodium salt in severe loss of gastric juice by vomiting is so great that excretion of both NaCl and $NaHCO_3$ is almost completely stopped in the apparent effort to preserve what is left of the body's store of sodium salts. In the absence of bicarbonate in the urine the pH falls toward that of a solution of free H_2CO_3.

Sodium chloride infusions correct the alkalosis and dehydration, replace the lost plasma sodium and chloride, and permit excretion of the excess $NaHCO_3$ which then raises the urine to alkalinity (pH 7.5 to 8.0). Since other base is also lost under such conditions, K, Ca, and Mg should be used in addition to Na.

A summary of the mechanisms regulating the reaction of the blood have been described by Carl Schmidt in the following discussion:

"The fundamental facts are these: In order that the cells of the body may function normally, they must be surrounded by a liquid environment (tissue fluid and lymph) with a reaction slightly on the alkaline side of neutrality. This reaction is maintained constant in spite of wide fluctuations in the amounts of acid and alkali taken into the body with the food and in the amounts of acid produced by the metabolic processes of the body. The factors responsible for this constancy fall into two main groups: (1) *physicochemical*, and (2) *physiological*. The various factors of the two groups cooperate in such ways that a change in one physicochemical factor is compensated ('buffered') by other factors of the same group, and if this proves insufficient physiological factors are brought into activity to restore the reaction of the blood to normal.

"The range of the reaction of the blood serum compatible with life in man appears to be about from pH 7.0 to pH 7.8, but these are the extreme limits encountered in very abnormal conditions. In normal persons the range is much narrower; i.e., the acidity of the serum varies only between pH 7.4 and pH 7.6; under ordinary circumstances the serum remains at about pH 7.4, and if alkalosis is produced (as by overventilation) symptoms of that disturbance (tetany) appear when or before pH 7.6 is attained."

The *physicochemical* factors, Schmidt goes on to say, are the buffers. (Buffers are *substances which prevent changes in the pH of* a solution when an acid or alkali is added.) Chief among the buffers of the blood are the dissolved CO_2 and the basic bicarbonates which are in equilibrium $CO_2/BHCO_3$). The carbon dioxide-bicarbonate buffer system is important quantitatively because it serves as a means of neutralizing

more than 60 per cent of the acids other than carbonic which enter the blood (it cannot of itself neutralize CO_2) and important qualitatively because the CO_2 is volatile and can be eliminated from the lungs (owing to the sensitivity of the respiratory center, an increased tension of CO_2 in the blood increases pulmonary ventilation). "Consequently the amount of bicarbonate in the blood gives a trustworthy picture of the amount of alkali available to neutralize acid, i.e., the alkali reserve. . . .

"The great importance of bicarbonate as a defense against acid depends upon the fact that when another acid is introduced and bicarbonate is decomposed, its acid radical can be eliminated promptly by the lungs. For this reason as much as 80 per cent of the bicarbonate of the blood can be decomposed before severe acid poisoning results. But when the acid is carbonic—as it normally is—hemoglobin is the buffer of paramount importance."

"At the normal plasma pH of 7.40 the proportions of $CO_2/BHCO_3 = 1/20$." If an acid is injected in experimental animals the $BHCO_3$ is reduced, making the blood more acid—the CO_2 tension increases and breathing is stimulated. "CO_2 is thus removed until the ratio $CO_2/BHCO_3$ again becomes 1/20; although the actual amounts of $BHCO_3$ may now be considerably less than before, as long as the ratio remains unchanged the pH is unaltered." *Therefore, changes in acid or alkali content do not cause a change in the pH of the blood, except in cases where such changes are great and prolonged.*

The *physiologic* factors involved in regulating the acid-base balance are *pulmonary ventilation* and *renal excretion.* When acids appear in the blood during violent exercise (lactic acid); in severe diabetes or starvation (beta-hydroxybutyric and aceto acetic acid); or in anoxemia (lactic acid) the alkali reserve is depleted, the H-ion concentration of the blood increases, and the CO_2 tension rises. Breathing is stimulated, the CO_2 tension is reduced, and the ratio $CO_2/BHCO_3$ is restored to 1/20. At the same time the kidney excretes sodium acid phosphate (NaH_2PO_4). If there is an excess of alkali, due to the ingestion of alkali or the loss of acid (as in severe vomiting due to intestinal obstruction or in certain types of diarrhea) there will result a decrease in acidity, breathing will be slowed to allow CO_2 to increase in the blood, and the kidneys will eliminate base (Na_2HPO_4).

If the increase in acid is due to an accumulation of CO_2, bicarbonate is also increased. This is made available by the passage of chloride into the erythrocytes, which in turn yield their bicarbonate ions to the plasma. If the decrease in acid is due primarily to a loss of CO_2 (as at high altitudes, or in hyperpnea from other causes than an increased CO_2 tension in the blood) there is a relative excess of $NaHCO_3$, and this is excreted in part in the urine. *Therefore, an acidosis due primarily to retention of CO_2 is accompanied by an increased bicarbonate, and an alkalosis due to excessive loss of CO_2 is accompanied by a decrease of bicarbonate.*

"The *ammonia mechanism* makes NH_3 available for combination with abnormal acid, as in the acidosis of diabetes, instead of excreting the nitrogen as neutral urea. The ammonia neutralizes acid that would otherwise demand alkali of the blood and the latter is thus spared to some extent. When there is a relative excess of alkali in the blood, ammonia excretion diminishes or ceases and other alkali is excreted instead. This mechanism comes into play very slowly, i.e., after several days of acidosis or alkalosis." Carl F. Schmidt in Macleod's *Physiology in Modern Medicine.*

Acidosis and Alkalosis

Acidosis means excess acid in the body; *alkalosis* signifies excess alkali. Strictly speaking, true acidosis is present only when the blood is less alkaline than normal (pH below 7.4) and alkalosis when the blood is more alkaline than normal (pH above 7.4). Actually, however, there may be sufficient poisoning by acid or alkali excess to produce definite symptoms before the reaction of the blood has changed appreciably.

Therefore, the terms acidosis and alkalosis as we employ them do not necessarily imply a change in pH. As long as the hydrogen ion concentration of the blood remains within normal limits, the acidosis is *compensated*. When the poisoning becomes too severe for the defense mechanisms to compensate and the hydrogen ion concentration changes, the acidosis or alkalosis is *uncompensated* and the condition is usually a very serious one.

If the term acidosis is used to denote a fall in plasma bicarbonate and alkalosis a rise, then they are misleading words because where CO_2 is lost in excess there is a compensatory reduction of $NaHCO_3$ but this is not acidosis. Also if CO_2 is retained as in pneumonia there is a certain amount of compensatory increase in alkali reserve but this is not alkalosis. Therefore two new terms have been introduced: acidemia and alkalemia. Acidemia is a state in which the pH is lowered. Acidosis then is used to denote a lowered alkali reserve **with unaltered pH.** Alkalemia indicates a state in which the pH of the blood is raised. Alkalosis is used to mean an increase in the alkali present with or without a **change in pH.** In the discussion which follows the terms acidosis and acidemia are used to indicate excess acid, whereas the terms alkalosis and alkalemia indicate excess alkali.

Should the pH of the blood reach neutrality (pH 7.0), life would be endangered. However, it may deviate somewhat from 7.4. When the pH rises to 7.6, the patient is said to have an *alkalosis;* a rise to 7.8 would presage death. If the pH falls to 7.2, *acidosis* is said to exist. Since the blood is normally alkaline there is in a normal individual enough alkali available to neutralize considerable amounts of acid. This is called the *alkali reserve* and is used to denote the amount of base in the blood available for neutralization of fixed acids, lactic, hydrochloric, etc. It may be measured by determining the amount of base which is bound as bicarbonate. There is a large quantity of base (sodium, potassium, calcium, and magnesium) which is bound as salts or fixed acids (NaCl) and is not available for the neutralization of acid.

If we can measure the amount of plasma bicarbonate we know how much acid (aside from CO_2) is entering the blood. If acid is increased, there is less bicarbonate; if decreased, there is more. Normal plasma bicarbonate varies between 53 and 75 volumes CO_2 per cent. Free CO_2 is about 1/20 of this, or 2.5 to 3.5 volumes per cent. Normal acid-base balance implies H_2CO_3, $NaHCO_3$, and pH normal.

Clinical states in which there is a disturbance of acid-base balance have been summarized by Van Slyke as follows:

1. *Uncompensated Alkali Excess.*—$NaHCO_3$ is increased without a proportionate rise in H_2CO_3; pH is raised (alkalinity of blood is increased). The ingestion of large quantities of alkali (as in the treatment of peptic ulcer) or the loss of large amounts of hydrochloric acid by vomiting (as in pyloric obstruction) will produce alkalosis or alkalemia; in the former case, by increasing bicarbonate directly, and in the latter

case by increasing them indirectly as a result of lowering the acid. The loss of chlorides due to the persistent vomiting in intestinal obstruction causes the formation of more bicarbonate to maintain the normal osmotic pressure. Therefore the alkalosis is due not only to the loss of HCl (reducing acidity) but also to an increase in bicarbonate. The cell is left without chlorides and therefore water alone (with glucose) could not help without the addition of sodium chloride (see Chapter 11).

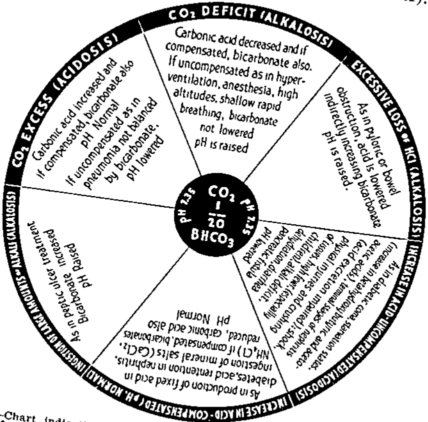

Fig. 103.—Chart indicating clinical causes of acidosis and of alkalosis. When the physiological factors compensate for increase or decrease in acid or base, the pH remains normal. If this mechanism fails, acidosis or alkalosis results.

2. *Compensated alkali excess* may be produced by the same causes as in 1. The bicarbonate is raised, but the carbonic acid also increases; therefore the pH remains normal.

3. *Uncompensated Alkali Deficit.*—The bicarbonates are reduced without a parallel reduction in carbonic acid. The pH is lowered, as in the acidosis of diabetic coma and in starvation states, where there is an increase in beta-hydroxybutyric and aceto-acetic acid, and in the terminal stages of nephritis, where acid exertion is greatly impaired. Shock, physical injuries and crushing of tissues, and high fever (especially in children) also cause an alkali deficit with acidosis.

4. *Compensated Alkali Deficit.*—The bicarbonates are reduced and the carbonic acid also; therefore the pH remains normal. This may occur when there is an abnormal production of fixed acid, as in diabetes, or in

a retention of acid, as in nephritis, or an ingestion of mineral acids or acid-producing salts ($CaCl_2$, NH_4Cl). Compensatory adjustments are seen in the increased acid and ammonia excretion in the urine and the lowered CO_2 tension in alveolar air.

Alkali deficit also results from an increased excretion of base, such as may occur in dehydration (see Chapter 11), pancreatic fistula, diarrhea, etc.

5. *Uncompensated CO_2 Excess.*—Carbonic acid is increased and the increase is not balanced by a proportionate increase of bicarbonate. The pH is lowered (acidosis or "gaseous acidosis" or acidemia). This imbalance *is seen in conditions where CO_2 excretion is interfered with, as in* pneumonia.

6. *Compensated CO_2 Excess.*—H_2CO_3 is increased but there is a proportional rise in $NaHCO_3$; pH is normal. This is seen where there is retention of CO_2 as in emphysema.

7. *Uncompensated CO_2 deficit* may occur as a result of hyperventilation (during anesthesia, in hot baths, at high altitudes, or in shallow rapid breathing from any cause). Carbonic acid is reduced but bicarbonate is not lowered to a corresponding extent; therefore the pH is raised (alkalosis or alkalemia or "gaseous alkalosis").

8. *Compensated CO_2 Deficit.*—The carbonic acid is reduced and also the bicarbonate; therefore, the pH is normal. The causes are the same as mentioned in 7 but less severe. The excretion of bicarbonate by the kidney is much slower than the excretion of CO_2 by the lungs, so the CO_2 deficit is soon compensated. The reduction of CO_2 from rapid or forced breathing has been called acarbia by Henderson. There is some doubt about acarbia being the sole cause of apnea during anesthesia, even though the administration of CO_2 usually corrects the condition. Hyperventilation during anesthesia produces a respiratory alkalosis, CO_2 tension in the arterial blood is reduced, and systolic and diastolic pressures fall somewhat, but this is transient; there may be tetany.

Symptoms and Signs.—The symptoms of acidosis include those of the primary disease causing it and dyspnea. In diabetic acidosis (due to ketone bodies) the dyspnea may be so severe as to resemble the "air hunger" following a severe hemorrhage. In addition there is usually polyuria, excretion of acid (in diabetes, of acetone, as well), and an increase in urinary ammonia. The laboratory shows a decrease in the CO_2 combining power of the blood (that is, a decrease in the CO_2 present as bicarbonate below the normal level of 50 volumes per cent).

One hundred cubic centimeters of arterial blood yields 48 c.c. of CO_2; 45 c.c. of this is in chemical combination (mostly bicarbonate). Venous blood contains about 52 to 70 c.c. of CO_2. By measuring the total CO_2 in a sample of acidified blood and then subtracting the free CO_2 (about 3 volumes per cent), the combined CO_2 is obtained.

Alkalosis would probably show, in addition to the symptoms of the primary disease, a depressed respiration (the alveolar CO_2 tension tends

to rise), excretion of base in the urine, and decrease of urinary ammonia. If the blood becomes definitely alkaline (pH 7.6), tetany may occur. The CO_2 combining power would rise to above 75 volumes per cent (due to an increase in the plasma bicarbonate).

"Air hunger" occurs in various states but is seen principally in diabetic coma and in severe hemorrhage see (Chapter 13). In the former it is due to an acidotic stimulation of the respiratory center chiefly by the acetoacetic acid which also depresses the higher centers of the brain, producing dyspnea with deep labored respirations. In the latter the respiratory center becomes more sensitive because of anemic anoxia: this leads to increased respirations. Cyanosis may be absent in either case (Chapter 19) for it depends on the amount of reduced hemoglobin present in the peripheral vessels.

Treatment of Acidosis and Alkalosis.—The treatment of these conditions is, of course, the elimination of their cause wherever possible. While this is being done, emergency measures are necessary. In pneumonia, oxygen is administered; in diabetes, insulin, etc. The introduction of chloride (as physiological salt solution) in hypochloremic states (such as intestinal obstruction) is a life-saving measure.

Isotonic salt solution is also useful in any acidotic state. It is true that an excess of chloride is present in physiological saline but if the kidneys are normal, this will be eliminated, leaving sodium to combine with carbon dioxide. Severe acidosis may be treated with sodium racemic lactate. One-sixth molar sodium lactate is isotonic, and is made by adding one part of molar sodium lactate solution to five parts of distilled water. About 10 c.c. of solution per kilogram of body weight is required to raise the CO_2 content of the blood 10 volumes per cent (Talbott).

Where much base is lost, as in severe diarrhea, Ringer's solution is perhaps best. In all conditions 5 per cent glucose in distilled water is indicated because of its food value (which counteracts acidosis and ketosis) and its water value (which prevents salt block and dehydration). It may also be given with physiological saline and is especially useful in this way for the treatment of postoperative subhydration and acidosis. Glucose, 0.8 Gm., may be utilized per kilogram per hour. There are only about 100 Gm. of glycogen in the liver of the average man and this would only supply enough sugar for about five hours. In shock and hypoproteinemias of any kind, blood transfusion is the treatment, not only because it restores osmotic pressure, but because the plasma and blood cells contain buffer substances. When large quantities of saline or glucose solutions are used, the osmotic pressure may be decreased greatly. Therefore blood should be used in conjunction with crystalloid solutions. It therefore may be given in any condition. Alkalosis is best treated by physiological saline solution if dehydration is present. Alkalosis caused by excessive loss of CO_2 (from hyperventilation or shallow rapid breathing, as seen during anesthesia) is best treated by the inhalation of CO_2 (7 to 10 per cent or more, depending on the degree of acarbia). A simple practical way to evaluate the need of CO_2 is to give it for one minute. If a seriously high blood CO_2 is present, respiration will be further depressed. If not, it will be stimulated.

The total quantity of body fluid is roughly 70 per cent of body weight. The amount of electrolyte needed to restore a patient to normal may be calculated as follows:

In a man weighing 100 pounds, there is approximately 35,000 c.c. of fluid ($500 \times 70 = 35{,}000$); 20 per cent of this is in the extracellular compartments (15 per cent is interstitial fluid and 5 per cent is blood plasma), making a total of 7,000 c.c. of fluid outside of the cells. Since this intercellular fluid is more readily analyzed than the intracellular component and since it represents the fluid medium in which the cell must live, it is used as an indicator of electrolytic requirements. Thus if the man has a hypokalemia we may arrive at his deficiency by determining the meq./L. of potassium which, let us say, is 3. The normal is about 5 meq./L. of potassium, or a total of 35 meq. There is, therefore, a deficit of 14 meq. in the extracellular compartment, or 2 meq./L. The conversion back to mg. per liter is as follows:

$$\text{meq./L.} = \frac{\text{X} \times \text{Valence}}{\text{atomic wt.}} \text{ or } 2 = \frac{\text{X} \times 1}{39} \text{ or X} = 78$$

Since there were 7 liters of extracellular fluid, there is a deficit of 7 × 78, or 546 mg. of K. The patient should receive about .5 Gm. of KCl by hypodermoclysis in addition to his daily requirement, caused by urinary loss (1.5-2.0 Gm.), or a total of 2.5 Gm. This should be given in sufficient fluid to restore water balance as described in Chapter 11.

This should correct his K deficit provided no further abnormal loss of K occurs. The urinary K should be determined to see whether or not this base is properly conserved by the kidneys.

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Chapter 13

HEMORRHAGE

Blood is the medium through which the estimated 23 million millions individual body cells receive their nourishment and oxygen and give off their secretion or excretion and carbon dioxide. It is composed of cells and plasma, 45 per cent of the former and 55 per cent of the latter. Its composition has been likened to the sea water of that early age when terrestrial animals first evolved, and its functions include all of the requirements of a subsisting environment; namely, respiratory, nutritive, excretory, maintenance of water content of the tissues through the capillary walls, regulation of body temperature through its water content and that of the tissues, protection against disease by its antibodies, and regulation of body functions through its connections between organs. These functions are seriously interfered with when there is a great loss of blood.

The cellular part of the blood is made up of erythrocytes, leucocytes, and thrombocytes (red cells, white cells, and platelets). The blood cells are formed principally in the bone marrow, which at any one time may be seen to contain 75 per cent white cells and 25 per cent red cells. The larger production of white cells is necessary because the red cells live from thirty to forty days and are destroyed by wear and tear, whereas the white cells live only a few days and are used up in their constant fight with bacteria and foreign bodies. Vierordt states that there are about twenty-three million millions red blood cells in the huduction of cells by the bone marrow. Acute erythemia is due to the 166, so that the blood contains only about thirty-three thousand million white cells. The erythrocyte contains hemoglobin which transports oxygen in sufficient quantity to maintain life, yet it loses its own nucleus early in its existence, uses no oxygen itself, and has no metabolism of its own. In a sense it is inanimate. A million million (1×10^{12}) red cells are formed daily by 1,400 c.c. of bone marrow largely in the ribs, skull, and vertebrae. During embryonic life they are formed in the liver, spleen, and bone marrow. In the adult they are formed in the bone spaces outside the dilated capillaries. When a sufficient number of cells have developed they break through the capillary walls presumably between the endothelial cells which quickly seal off the openings. White cells get into the blood stream in a similar manner but are capable of ameboid movement and may get into or out of the capillaries on their own power. Over a trillion red cells are destroyed daily. The reticulo-endothelial cells, largely of the spleen, remove them. Incidentally any red cell which is abnormal is removed by the spleen. Therefore, in certain anemias (sickle cell, spherocytosis) where an abnormal cell carries

on the functions of the normal erythrocyte, even though it is in a poor way, it is desirable to retain them; therefore splenectomy may be necessary. With the destruction of the red cells 25 Gm. of hemoglobin is destroyed daily and 100 mg. of iron is released, of which 85 mg. is used again; the rest is replaced by food. Five hundred cubic centimeters of bile, *containing about 350 mg. of bile pigment, is formed and excreted* by the liver.

WHOLE BLOOD = 1/11 th OF BODY WEIGHT

PLASMA ··· 55% by volume of blood

Water · · · · · · · · · · · · · 90 gms. per 100 cc.

Serum Albumin (From Liver) · · 4.1 gms. per 100 cc.

Serum Globulin · · · · · · · · · 2.7 gms. per 100 cc.
(From Liver and Reticuloendothelial Cells)

Fibrinogen (From Liver) · · · · 0.27 gms. per 100 cc.

Other Constituents : Non-protein nitrogen, glucose, chlorides, bicarbonate, magnesium, phosphorus, sodium, potassium, calcium.

CELLS ···· 45% by volume of blood

Red Blood Cells · · · · · · · · 4,500,000 - 5,000,000
(From bone marrow, mostly ribs - live 30-40 days. Destroyed by wear. Contain: Water, 60%, Hemoglobin, 38%, Other Proteins, 1%, also Chlorides, Lecithin, Cholesterol, Urea, Creatinine, Amino-acids.)

White Blood Cells · · · · 5,000 - 10,000 per cubic mm.
(From bone marrow, live only a few days. Lost in defense against bacteria.)

Lymphocytes · · · · · · 15 - 20% of white blood cells
(From lymph nodes and lymphoid tissue. Live 24 hrs. Pass into lumen of bowel.)

Fig. 104.—Composition of blood.

Each cell is about 7/25,000 of an inch in diameter and 2/25,000 of an inch thick and makes about 85 thousand complete trips from lungs to tissues during its life.

The number of red cells is increased in high altitudes, after muscular exercise, sudden increase in environmental temperature, and any condition which lowers the oxygen tension of arterial blood. The increase in the foregoing instances is absolute and comes from a release of red cells

which are stored chiefly in the spleen, and also from an increased production of cells by the bone marrow. Acute erythemia is due to the former, slow increase, to the latter cause.

Relative increase may be caused by a reduction in the amount of plasma or water. (See Chapter 11.)

Pathological conditions causing an *increase* in the number of red cells (polycythemia) are polycythemia vera; lung diseases which interfere with proper oxygenation, such as emphysema, tracheal, or bronchial stenosis, pneumothorax, or pulmonary tuberculosis in some instances; congenital heart disease, especially the tetralogy of Fallot because of pulmonary artery stenosis not in patent ductus; pulmonary arteriosclerosis (pulmonary hypertension), chronic carbon monoxide or chemical poisoning (arsenic, phosphorus, etc.).

Pathological states causing a decrease (anemia) are numerous and often not entirely clear. In general there may be a lack of adequate production (primary anemia) or an increase in destruction over production (secondary anemia). A relative anemia may occur due to increased retention of water in the body (hydremia).

Lymphocytes are formed in lymphoid tissue, chiefly lymph nodes, and live twenty-four hours and most of them are lost in the lumen of the bowel.

Leucocytes are lost in large numbers daily, and in *infections great numbers are produced and lost; often the bone marrow cannot make them fast enough and immature cells are furnished.* If destruction is rapid and in large amounts, pus is formed. Normally the dead leucocytes are removed by the reticulo-endothelial system. (See Chapter 4.)

Blood platelets are derived from the cytoplasm of megakaryocytes which in turn are formed in the bone marrow. They are about one-third the size of a red blood cell and number about 200,000 to 400,000 per cubic millimeter. Their chief function is in connection with blood clotting which will be discussed later in this chapter. They are increased after a meal of meat, during convalescence from infections, in certain allergic conditions, and in myeloid leucemia. *They are decreased in aplastic and pernicious anemia, lymphatic leucemia,* anaphylaxis, and the purpuras (symptomatic as seen in acute infections and idiopathic or purpura hemorrhagica). They are altered in hemophilia.

The fluid part of the blood is composed of plasma which is said to form originally from the secretion or actual solution of cells in the outer layer of the primitive endothelium. Plasma without fibrinogen is called serum. Therefore, plasma proteins include fibrinogen; serum proteins do not. These have been discussed in Chapter 11. *They constitute about 7 to 8 per cent of plasma. Over 90 per cent is water; the rest (about 2 to 3 per cent) is made up of potassium magnesium, etc.*; organic substances other than proteins (nonprotein nitrogenous material such as urea, uric acid, xanthine, hypoxanthine, creatine and creatinine, ammonia, and

amino acids); neutral fats, phospholipids, cholesterol and glucose; *hormones, antibodies, enzymes, amylases, lipases, esterases, proteases, etc.* The average human adult has about 1/11 of the body weight in whole blood and about 1/20 of the total body weight in plasma; this is, 9 and 5 per cent, respectively; that is, 90 c.c. per kilogram (or about 41 c.c. per pound) of body weight in whole blood and 50 c.c. per kilogram (or about 23 c.c. per pound in plasma). Infants have more blood in proportion to body weight.

There is also a relation between blood volume and body surface—it amounts to about 3.3 liters per square meter (Rowntree). This relationship is used on a per cent basis in plasma replacement of burns (Chapter 6). Blood volume may be determined by the dye method, Congo red or Evans blue T-1842. Gregersen developed a method of determining blood volume which is simplified. The steps are as follows: (1) The plasma concentration of the dye T-1824 is measured with the portable decade photometer designed by Nickerson. (2) The total plasma volume is obtained from the dye concentration in a single blood sample drawn ten minnutes after the dye injection. (3) The critical and troublesome procedure of measuring out an exact amount of dye at the time of making the determination is eliminated by using ampules containing a *standard amount of dye solution of known concentration. This also* eliminates all calculations from the determination of total plasma volume. By reference to a chart the plasma volume is obtained directly from the decade photometer reading. The total blood volume is then calculated from the plasma volume and the hematocrit. (4) The hematocrit may be determined with the copper sulfate-specific gravity method instead of with a high-speed centrifuge.

Stroke volume may be ascertained by several methods. In clinical practice the ballistocardiograph is most commonly employed. For more accurate information the Fick principle or the breathing of a foreign gas such as nitrous oxide may be used. The Fick principle is based upon the difference between the oxygen (or CO_2) content of the arterial and that of the venous blood and the total oxygen used (or CO_2 eliminated). By testing alveolar air in the ordinary basal metabolism test, the amount of oxygen consumed per minute is determined. Say it is 250 c.c. The arterial blood contains 20 volumes of oxygen per 100 c.c.; the venous blood, 14 volumes of oxygen per 100 c.c.; therefore, 6 volumes of oxygen is given in the tissues. The cardiac output is $\frac{250}{6} \times 100$; that is, for every 100 c.c. of blood pumped by the heart, 6 c.c. of oxygen were used and 250 c.c. of oxygen were consumed per minute. Therefore, 4,166 c.c. of blood were pumped per minute. If the pulse rate is 72, then the stroke volume would be $\frac{4166}{72}$, or about 60 c.c. per beat.

The difficulty here is that to be accurate the venous blood should come from the right heart because cutaneous veins carry different con-

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Angiocardiography synchronized with timing devices and the electrocardiograph easily records circulation time from the vein used, through the right side of the heart, the lungs, the left side of the heart, and the aorta and depicts the relationship with heart cycles as registered in the electrocardiogram (see Chapter 17). *The total circulation time* from the antecubital vein of one arm through the subclavian, vena cava, right heart, lungs, left heart, aorta, subclavian artery, capillary bed, and back to the antecubital vein of the opposite arm is about 21 seconds by the fluorescein method; it varies between 12 and 26 seconds. Pulmonary circulation time (radioactive method) is about 11 seconds (5 to 17 seconds). The volume of blood in the lungs may be calculated by knowing cardiac output per minute and the pulmonary circulation time. The formula is: Cardiac output = 8 per cent total blood volume which is the average quantity of blood in the lungs $\times \dfrac{60}{\text{Pulmonary circulation time}}$

Blood moves at a fairly uniform rate through the pulmonary circuit but varies greatly in the systemic circulation. Circulation time is reduced in hyperthyroidism and in anemia and prolonged in myxedema, polycythemia, cardiac failure, and postoperatively up to 5 per cent by the tenth postoperative day. The latter may be a factor in postoperative phlebothrombosis. The velocity in the larger arteries is about 200 times that of the capillaries. *Blood moves through a closed system* (with the possible exception of the spleen) whose capacity bears a dirct relationship with the volume of blood it contains. Should the volume become greater or smaller, the size of the vascular system varies with it (vasodilation and vasoconstriction). Moreover, the volume is diminished or increased by the compensatory mechanisms to be described. *Should these mechanisms fail, shock follows which tends to conserve* and utilize the volume of blood which remains.

COAGULATION OF BLOOD

Prothrombin + Ca ions + thromboplastin = Thrombin
Thrombin + fibrinogen = Fibrin

Prothrombin is produced chiefly in the liver. Vitamin K is necessary for its formation. Vitamin K (a methyl phytyl naphthaquinone) comes from food (K_1) and from the action of bacterial flora of the large intestines (K_2). Bile is needed for absorption. If there is no bile (as in obstructive jaundice), if coliform bacteria are absent as after succinylsulfathiazole, Sulfathalidine, or streptomycin, administration, if the bowel wall is diseased as in ulcerative colitis and sprue so that absorption cannot occur, or if the liver is diseased so that it cannot use it, a hypoprothrombinemia may occur. Prothrombin is a protein body normally present in concentration of 0.03 per cent or 35 mg. per 100 c.c. of blood. It is constantly being formed and used so that one test is not of

centrations of oxygen. This requires cardiac catheterization (see Chapter 17). Hill has used the hemoglobin content (15 Gm.) to determine arterial blood oxygen and has guessed at venous blood oxygen content based on previous experiments. Calculations would be as follows: 1 Gm. of hemoglobin unites with 1.34 c.c. of oxygen when fully saturated. The O_2 capacity of the blood is 15×1.34, or 20 c.c. Since the arterial blood is about 95 per cent saturated, the O_2 content is about 19 c.c. The amount of oxygen consumed per minute is determined by basal metabolism test. The average venous blood oxygen is known (about 14 volumes of oxygen per 100 c.c.); the amount consumed per minute can be determined as previously described. Say 250 c.c. of oxygen is consumed per minute. The formula would be $\frac{250}{5} \times 100$ or 5,000 c.c. of blood pumped per minute.

The minute volume of the heart normally is between 3,500 to 4,600 c.c. It is fairly constant for a given individual but varies in different people. The minute volume per square meter of body surface is 2,200 c.c.—cardiac index. Therefore, cardiac output is proportional to the basal metabolism which may be predicted along with the former from the surface area. Stroke volume is from 60 to 70 c.c. Cardiac output is increased with strenuous muscular exercise, high environmental temperatures, after a heavy meal, during emotional excitement and pregnancy, and in increased CO_2. It is also increased in abnormal conditions such as hyperthyroidism, anemia, fever, and arteriovenous fistula (although this is questioned by some); it is decreased in cardiac irregularities, organic heart disease, cardiac tamponade, myxedema, pneumothorax, and shock.

CIRCULATION TIME

The time which a red blood corpuscle takes to make the complete round of both the systemic and pulmonary systems is the total circulation time; the pulmonary circuit alone is the pulmonary circulation time. The former may be tested in many ways. If the patient is cooperative, 2½ Gm. of solubule saccharine in 2 c.c. of distilled water may be injected intravenously and the first taste of sweetness is recorded; the same may be done with Decholin and a bitter taste noted. If the patient cannot cooperate, the dye fluorescein may be injected into the arm vein of one side and its arrival at five-second intervals in the corresponding vein of the other arm timed, or histamine may be injected intravenously (0.001 mg. histamine phosphate per kilogram of body weight) and the exact time at which a flushing of the face occurs noted. The pulmonary circulation may be determined by injecting 0.11 mg. of sodium cyanide per kilogram of body weight into the arm vein. Since cyanide stimulates respirations through its action on the carotid sinus, the effect may be recorded by a pneumograph using a stop watch.

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great value. Consumption or disappearance of prothrombin takes place in the lungs. Platelets undergo disintegration in the capillaries and lungs. Since prothrombin and fibrinogen are constantly produced, it may be assumed that through the action of prothrombin, thromboplastin is converted into fibrin, possibly to protect the integrity of the capillary walls (Howell). The prothrombin response to Vitamin K therapy has been used as a liver function test and as a diagnostic aid in differentiating between intrahepatic and obstructive jaundice. (Chapter 22.)

Thrombokinase or *thromboplastin* is produced from platelets, is also present in all tissues, and is closely allied to cephalin. Thrombokinase alone acts slowly; however, this is not true when it is combined with ionized calcium. Prothrombin is activated by thromboplastin to produce thrombin.

Thrombin (an enzyme) acts on soluble fibrinogen to produce insoluble fibrin which enmeshes blood cells to produce clot. Fibrinogen is produced chiefly in the liver (see Chapter 12).

Blood remains fluid in vessels for two reasons: (1) there is very little thromboplastin present and therefore the active enzyme thrombin is not produced; (2) should thrombin form, a normal antithrombin is present to inactivate it. This antithrombin is thought to be a heparin-albumin compound whose presence is ensured by the constant secretion of heparin into the blood in small amount. Heparin is found in the liver, lung, muscle, and intestinal wall, and, to a lesser extent, in the spleen, heart, and thymus. Heparin is produced in the basophilic mast cells which are found mainly in blood capillaries. Heparin by itself is not an anticoagulant and when added to blood it reacts with some constituent to neutralize thrombin if present or to prevent the conversion of prothrombin to thrombin, or both. In addition, it has anticoagulant properties because it prevents the agglutination of platelets which is the starting point of thrombus formation. Chemically heparin is a mucoitin polysulfuric ester. It is said to act at various sites in the process of coagulation. We have seen that thromboplastinogen plus the activating enzyme from the platelets (thrombokinase) produces thromboplastin. Thromboplastin plus prothrombin plus calcium produces thrombin. (Accelerator globulin is a plasma factor which accelerates the activation of prothrombin in the presence of thromboplastin and calcium ions.) Thrombin plus fibrinogen produces fibrin. Heparin is said to act in the following ways:

1. By the inhibition of platelet agglutination, thereby reducing the amount of thrombokinase.
2. By interfering with the thromboplastin-prothrombin reaction through antithromboplastin and antiprothrombin.
3. By interfering with the action of thrombin and fibrinogen through antithrombin.

Coagulation time must be checked frequently when heparin is being used. The best method for checking *coagulation time is the Lee-White method which is done as follows:*

Puncture the vein with a small needle and syringe and collect 1 c.c. *of blood without using suction. Note the time. Remove the needle from* the syringe and empty the blood into a clean test tube of 8 mm. diameter. Place the tube in a water bath with a temperature of 75° F. or in a room where the temperature is between 65 and 90° F. Tilt the tube at one-minute intervals and note the time when coagulation has taken place, permitting inversion of the tube. The normal by this method is five to ten minutes. After heparin this is prolonged to thirty to forty-five minutes.

The normal coagulation time is about two and one-half to three minutes. If blood is kept constantly stirred, fibrinogen is converted to fibrin which in turn is removed or clings to the stirring rod. That which remains is serum and cells which do not clot. This apparently is the reason that blood in the pleural cavity remains liquid: it is defibrinated and the fibrin adheres to the visceral and parietal pleura.

ABNORMAL STATES

Bleeding tendencies are due to a prolonged clotting or bleeding time. Hemorrhagic diseases due to *coagulation defects* may be outlined as follows:

Thromboplastin Deficiency

Thromboplastin deficiency is the most probable cause of hemophilia (Howell) and is said to be due to an abnormal resistance of the platelets which are unusually sturdy. Since platelets are formed from the cytoplasm of megakaryocytes, these too must be abnormal. Hemophilia is a hereditary disease which is essentially a dysfunction of the megakaryo-*cytes. Bleeding time is normal. Thromboplastin should control the* prolonged coagulation time but does not since it is not available in pure form. Blood and plasma help restore normal coagulation due to the thromboplastin in such blood. We have performed emergency operations on persons with true hemophilia successfully with the aid of plasma and blood transfusions.

Although there is no proof of pseudohemophilia, there are male and female subjects who have a prolonged clotting time which may be dangerous. The condition is congenital and is usually known to the patient. It is not due to any other deficiencies except thromboplastin which is slow in being produced. Perhaps these people have less tough platelets than do those with hemophilia. They respond to such agents as oxalic acid or sodium citrate which may make platelets more vulnerable.

Prothrombin Deficiency

Inadequate supply of vitamin K may give rise to hemorrhagic disease, especially in the newborn. In such cases vitamin K is specific.

Faulty absorption of vitamin K may be due to absence of bile (obstructive jaundice or biliary fistula), severe disease of the intestine preventing absorption (sprue, gastrocolic fistula, ulcerative colitis), or succinylsulfathiazole, Sulfatholidine, or streptomycin, inhibiting the coliform bacteria. Vitamin K and phthiocol (intravenously) are useful.

Prothrombin deficiency may result from inability of liver to utilize vitamin K for synthesis of prothrombin as seen in prolonged obstructive jaundice, severe hepatitis, cirrhosis, hemorrhagic disease of cattle, and drugs such as salicylates and Dicumarol. Vitamin K is useless unless the liver is improved. Intravenous glucose, calcium, and, in cirrhosis, 1.5 to 3 Gm. choline and the same amount of cystine daily, supplemented with 3 to 45 Gm. of Brewer's yeast and a high protein diet, may help improve liver function.

Fibrinogen Deficiency

Fibrinogen deficiency may be acquired due to liver diseases, nutritional deficiency disease, and extensive destruction of bone marrow; it may also be congenital. Blood transfusion is the only treatment except in liver disease (see Coagulation of Blood).

Calcium Deficiency

Calcium deficiency does not cause hemorrhagic disease. Calcium is useful in treatment due to its indirect action on the liver.

Excess of Antithrombin

Excess of antithrombin (heparin) is not present in normal blood; its presence in small amounts does not interfere with clotting mechanisms. Transient bleeding in anaphylactic shock is thought to be due to an outpouring of heparin. No treatment for this is necessary. Also rarely cholinergic drugs such as prostigmine may delay clotting.

Erythroblastosis neonatorum has been discussed in Chapter 10. It is probably due to the passage of anti-Rh agglutinins from the mother, who is usually Rh negative, to the fetus, who is Rh positive. The condition manifests itself clinically in various ways, such as generalized edema (hydrops), icterus, severe degrees of anemia, and hemorrhagic diathesis and may result in stillbirth. Destruction of red cells may be so fast that bile pigment fills the liver and its ducts, producing a jaundice due to hemolysis as well as obstruction by bile pigment. The treatment includes multiple transfusions with Rh-negative blood, vitamin K given intramuscularly, glucose given intravenously, and oxygen by inhalation. It is thus apparent that in this condition any or all of the factors interfering with normal coagulation may be present.

The clotting of blood may be hastened then by correcting factors which are preventing it, if possible. In addition, adrenalin intramuscu-

larly may help (normally shortened clotting time is noted from emotional excitement, muscular exercise, and hemorrhage—probably through the liberation of adrenalin). Thrombin and thromboplastin are useful, especially the newer products. These will be discussed later. Some snake venoms accelerate clotting due to their proteolytic enzyme which converts prothrombin to thrombin.

Prolonged Bleeding Time

Hemorrhagic states due to *prolonged bleeding* time are usually termed *purpura*. Since there are various causes for this disease, it is well to look upon it as a symptom of a disorder of the blood vascular tree because coagulation is normal. Purpuric spots or ecchymoses are seen in acute infections (scarlet fever, smallpox, diphtheria, meningo- and streptococcic septicemia), in scurvy, in leucemias, and various anemias, and in toxic reactions resulting from snake venoms, sulfonamides, etc. In some types there is a degeneration of the capillary wall; in others there is a thrombocytopenia, although low platelet counts are not always present. Perhaps the platelets repair or seal off weak points in capillaries and their reduction leaves wear and tear without restitution. Platelets may be destroyed too rapidly or are not produced in sufficient amounts as seen in aplastic anemia and leucemia.

The *types* of *purpura* are: (1) *Symptomatic* (a) which is not dependent on disturbance of the blood and (b) which is associated with thrombocytopenia. (2) *idiopathic:* (a) primary or anaphylactoid; in this group are Schönlein's disease (with joint manifestations) and Henoch's (with intestinal crisis). There is no specific treatment for these groups. If the *cause* can be found, it should be eliminated. (b) Thrombocytopenic (idiopathic purpura hemorrhagica, Werlhof's disease); treatment is splenectomy (see Chapter 22). (3) *Purpura fulminans*—a fetal disease with normal platelet count. The cause is unknown. An anticoagulant resembling heparin has been found in the blood of dogs that had hemorrhagic tendencies after prolonged exposure to x-ray. This bleeding may be prevented and temporarily stopped by the intravenous use of protamine sulfate or toluidine blue. This is thought to be due to the ability of these substances to render heparin inactive. Patients with thrombopenic purpura have an increase in a heparin-like substance and toluidine blue or protamine sulfate helps arrest bleeding in thrombopenic purpura. Titration of the patient's blood may reveal the presence of a heparin-like substance. These antiheparin drugs may then be used in preparation for splenectomy, in cases of acute bone marrow suppression, in leucemias, and in patients who have received too much heparin.

CLOTTING TENDENCIES

Intravascular clotting is discussed in Chapters 5 and 17 under thrombosis and Embolism. It should be reviewed in this chapter because of the use of anticoagulants and their relation to hemorrhage. Experi-

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Prothrombin deficiency may result from inability of liver to utilize vitamin K for synthesis of prothrombin as seen in prolonged obstructive jaundice, severe hepatitis, cirrhosis, hemorrhagic disease of cattle, and drugs such as salicylates and Dicumarol. Vitamin K is useless unless the liver is improved. Intravenous glucose, calcium, and, in cirrhosis, 1.5 to 3 Gm. choline and the same amount of cystine daily, supplemented with 3 to 45 Gm. of Brewer's yeast and a high protein diet, may help improve liver function.

Fibrinogen Deficiency

Fibrinogen deficiency may be acquired due to liver diseases, nutritional deficiency disease, and extensive destruction of bone marrow; it may also be congenital. Blood transfusion is the only treatment except in liver disease (see Coagulation of Blood).

Calcium Deficiency

Calcium deficiency does not cause hemorrhagic disease. Calcium is useful in treatment due to its indirect action on the liver.

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Excess of antithrombin (heparin) is not present in normal blood; its presence in small amounts does not interfere with clotting mechanisms. Transient bleeding in anaphylactic shock is thought to be due to an outpouring of heparin. No treatment for this is necessary. Also rarely cholinergic drugs such as prostigmine may delay clotting.

Erythroblastosis neonatorum has been discussed in Chapter 10. It is probably due to the passage of anti-Rh agglutinins from the mother, who is usually Rh negative, to the fetus, who is Rh positive. The condition manifests itself clinically in various ways, such as generalized edema (hydrops), icterus, severe degrees of anemia, and hemorrhagic diathesis and may result in stillbirth. Destruction of red cells may be so fast that bile pigment fills the liver and its ducts, producing a jaundice due to hemolysis as well as obstruction by bile pigment. The treatment includes multiple transfusions with Rh-negative blood, vitamin K given intramuscularly, glucose given intravenously, and oxygen by inhalation. It is thus apparent that in this condition any or all of the factors interfering with normal coagulation may be present.

The clotting of blood may be hastened then by correcting factors which are preventing it, if possible. In addition, adrenalin intramuscu-

larly may help (normally shortened clotting time is noted from emotional excitement, muscular exercise, and hemorrhage—probably through the liberation of adrenalin). Thrombin and thromboplastin are useful, especially the newer products. These will be discussed later. Some snake venoms accelerate clotting due to their proteolytic enzyme which converts prothrombin to thrombin.

Prolonged Bleeding Time

Hemorrhagic states due to *prolonged bleeding* time are usually termed *purpura.* Since there are various causes for this disease, it is well to look upon it as a symptom of a disorder of the blood vascular tree because coagulation is normal. Purpuric spots or ecchymoses are seen in acute infections (scarlet fever, smallpox, diphtheria, meningo- and streptococcic *septicemia*), *in scurvy, in leucemias,* and various *anemias,* and in toxic reactions resulting from snake venoms, sulfonamides, etc. In some types there is a degeneration of the capillary wall; in others there is a thrombocytopenia, although low platelet counts are not always present. Perhaps the platelets repair or *seal off weak points in capillaries and* their reduction leaves wear and tear without restitution. Platelets may be destroyed too rapidly or are not produced in sufficient amounts as seen in aplastic anemia and leucemia.

The *types* of *purpura* are: (1) *Symptomatic* (a) which is not dependent on disturbance of the blood and (b) which is associated with thrombocytopenia. (2) *idiopathic:* (a) primary or anaphylactoid; in this group are Schönlein's disease (with joint manifestations) and Henoch's (with intestinal crisis). There is no specific treatment for these groups. If the *cause* can be found, it should be eliminated. (b) Thrombocytopenic (idiopathic purpura hemorrhagica, Werlhof's disease); treatment is *splenectomy* (see Chapter 22). (3) *Purpura fulminans*—a fetal disease with normal platelet count. The cause is unknown. An anticoagulant resembling heparin has been found in the blood of dogs that had hemorrhagic tendencies after prolonged exposure to x-ray. This *bleeding may be prevented and temporarily stopped by the intravenous* use of protamine sulfate or toluidine blue. This is thought to be due to the ability of these substances to render heparin inactive. Patients with thrombopenic purpura have an increase in a heparin-like substance and toluidine blue or protamine sulfate helps arrest bleeding in thrombopenic purpura. Titration of the patient's blood may reveal the presence of a heparin-like substance. These antiheparin drugs may then be used in preparation for splenectomy, in cases of acute bone marrow suppression, in leucemias, and in patients who have received too much heparin.

CLOTTING TENDENCIES

Intravascular clotting is discussed in Chapters 5 and 17 *under thrombosis* and Embolism. It should be reviewed in this chapter because of the use of anticoagulants and their relation to hemorrhage. Experi-

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lar surgery to prevent thrombosis after injury of blood vessels, in trans-*plantation of organs, in exchange transfusion,* in coronary thrombosis produced by sclerosing agent, and in the prevention of peritoneal adhesion. Clinically it has been used in peripheral thrombophlebitis and phlebothrombosis, pulmonary embolism, mesenteric thrombosis, coronary thrombosis, cerebral thrombosis, thrombosis of the central vein of the retina, vascular surgery, postoperative prophylaxis against bacterial endocarditis (with penicillin), and in the laboratory for the Wassermann iso-agglutination and other tests. Heparin is best administered intravenously although it may be given by subcutaneous injection. The smallest effective dose to maintain blood coagulation at from fifteen to thirty minutes is desirable. Heparin has no effects on blood clots but will prevent further thrombi from forming (propagation thrombi). Usually 1,000 to 2,000 units per hour or from 10 to 20 mg. per 100 c.c. of fluid by venoclysis will be necessary. Heparin may be given by subcutaneous injection using Pitkin's menstruum which releases water-soluble drugs slowly. It is composed of 18 per cent gelatin, 8 per cent dextrose, 1 to 1.5 per cent acetic acid, and distilled water sufficient to make 100 per cent. *Heparin, 100 to 200 mg., is added to this menstruum with or with-*out the vasoconstrictors, 10 mg. of ephedrine and 1 mg. epinephrine. This mixture is available in 1 or 2 c.c. ampules. Pitkin's menstruum is effective but painful. Patients under 150 pounds (68 kg.) get 1 c.c. containing 100 mg. Heavier individuals get double the dose. Subsequent doses depend on the response. Prothrombin time as well as coagulation time should be taken every twelve hours. If the former is prolonged, vitamin K may be necessary after the use of Dicumarol, since it takes Dicumarol two to five days to act. This drug may be given at the same time that the heparin solution is injected. The latter takes only one and one-half to two hours to act and prolongs coagulation time for twenty-four to forty-eight hours if given without vasoconstrictors. If given with them, the action of heparin lasts about sixty hours. A Howell unit is defined as the quantity of heparin which will prevent the clotting of 1 c.c. of cat's blood kept cold for twenty-four hours. For transfusion the donor is given ¾ to 1 mg. per kilogram of body weight. After heparin is discontinued, the coagulation time returns to normal in a few hours. *Protamine* given intravenously hastens its return to normal because it is a strongly basic protein and heparin breaks its combination with the albumin factor in favor of the more strongly basic protein protamine, thus releasing thrombin. Whole blood or plasma may also be used for this purpose.

Some people are sensitive to heparin, others are resistant. The latter are seen in (a) early postoperative period, (b) following cardiovascular accidents (coronary thrombosis, thrombosis, cerebral hemorrhage), (c) Buerger's disease.

Heparin is available in two types: the aqueous solution which may be used intravenously and which produces a high concentration but has

mentally coagulation may be produced by (1) by the injection of thrombin (this is *transient and may be followed by* a negative or prolonged coagulation time); (2) by the injection of *thrombokinase (from lung,* thymus, and lymph nodes); if continued the fibrinogen is used up and clotting is delayed; (3) by injury of the vessel. Clinically it is seen due to (1) injury to the vessel: (a) *outside* the vessel at surgery, during forceps delivery, by inflammation around the artery or vein, and by new growth; (b) *inside* the vessel by trauma produced by hypertonic solutions or the *needle in continuous venoclysis, by infections* such as pneumonia, etc., or by toxins as in eclampsia and burns; (2) changes in the rate of flow; this is especially serious because it is silent without symptoms (phlebothrombosis) and normally occurs in the veins of the lower legs following complete immobilization; (3) changes in the density of the blood in dehydration, starvation, etc.; (4) chemical changes as in anoxemia; *from large doses of digitalis and adrenalin through nervous stimulation or injection.*

Anticoagulants

Blood *clotting is inhibited by* : (1) *Cold due to its effect on clotting* enzymes. Therefore, stored blood is kept at 5 to 10° C.; this also retards bacterial growth if there is contamination. Ultimately the blood clots. Cold decreases bleeding on the body surface due to vasoconstriction. (2) Avoidance of contact between blood and injured tissues or rough surface which prevents clotting for a time. The well-known *fact that a wound made by a sharp instrument bleeds more than one* by a blunt force provides for less platelet disintegration in the former and more in the latter. The old Kimpton-Brown method of transfusion was accomplished by using paraffinized glass cylinders to avoid a rough surface. (3) Decalcification, where the addition of sodium oxalate (or potassium or magnesium) or a fluoride (0.1 per cent) *to blood will prevent clotting.* Calcium oxalate is formed in the former instance. Sodium citrate also prevents clotting in vitro (not in vivo) by forming calcium sodium citrate. If calcium chloride is added, the blood clots again; also the addition of thrombin or thromboplastin will do this. (4) Neutral salts such as magnesium sulfate, 27 per cent solution, *mixed 1 part to 4 of blood;* also sodium sulfate, 10 per cent solution, mixed with equal parts of blood. (5) Azo dyes (Chicago blue, 6 B, trypan red, trypan blue, etc.). (6) Biological products: (a) hirudin from leeches, (b) snake venoms, (c) peptone solution, (d) cysteine, (e) heparin, (f) Dicumarol.

Heparin and Dicumarol have important *clinical applications.*

Heparin.—The nature and source of *heparin has been briefly* discussed. Its *action* is based on an inhibitory effect on prothrombin, or the first stage of coagulation, and on thrombin to prevent the second stage. The presence of a component of the serum-albumin fraction is necessary before heparin can assert its action. Heparin and thrombokinase are antagonistic. *Heparin has been used experimentally in* vascu-

hours, but if the fortified heparin has been used, it takes approximately twenty-four to forty-eight hours for the coagulation time to again become normal.

Heparin may be used in doses sufficient to prolong coagulation up to sixty minutes; however, usually thirty to forty-five minutes is considered adequate. It, of course, should not be used in blood dyscrasias or recent *operations on the spinal cord where bleeding might result in very* serious consequences or before surgery. In cases with ulcerative lesions or open wounds or where drainage tubes are used, as in the renal pelvis or the common bile duct, or with indwelling catheters or tubes in the nose and mouth, the risk of bleeding is great and, therefore, heparin should be used with extreme caution. Since the effect of heparin is prompt and that of Dicumarol is delayed, some surgeons prefer to use heparin to get the immediate effect and then fortified heparin or Dicumarol to get a delayed effect. As we shall see, Dicumarol is a drug with considerable danger because of its toxic action on the liver; therefore, the trend at present is to rely more upon heparin than upon Dicumarol. However, the ease of administration of Dicumarol has made it the drug of choice where treatment must be continued over a long period of time.

Dicumarol.—AP or antiprothrombin was the name given by Swedish biochemists for 3,3′-methylene bis (4-hydroxycoumarin) or Dicumarol because it was thought to inactivate or destroy prothrombin. By studying the hemorrhagic disease in cattle resulting from the ingestion of spoiled sweet clover, the active principle Dicumarol has been isolated. Its anticoagulant effect is due to a depression of synthesis of prothrombin *rather than a direct effect on this substance. Although there is no* destruction of liver tissue or reduction in any other function, there is an effect on prothrombin production. The return of prothrombin levels to normal may be speeded by the administration of vitamin K_1 oxide. This is due to either a neutralization of the toxin or the synthesis of prothrombin *in the presence of excess vitamin K. Salicylates* may cause hypoprothrombinemia and this can be prevented or counteracted by the administration of synthetic vitamin K. Dicumerol is useful in many of the states in which heparin is employed. Thus it may be employed prophylactically after operations likely to be followed by thrombosis and embolism such as splenectomy and pelvic operations; in surgery of the blood vessels (traumatic injuries, removal of the thrombus or embolus); as a therapeutic measure in phlebothrombosis, phlebitis, and thrombophlebitis in the extremities; thrombosis or embolism in pulmonary vessels, coronaries, and mesenterics; also in blood transfusion and laboratory work. Its great advantage over heparin is its ease of administration. It should not be used in the presence of liver disease. The dose is usually 200 to 300 mg. daily until the prothrombin time has reached 35 seconds, and then 50 mg. daily thereafter. After discontinuation the prothrombin time may be prolonged for two to three days. Heparin and Dicumarol may be used simultaneously.

a transient effect and the so-called fortified heparin which is procurable as Heparin Pitkin Menstruum or Depo-heparin sodium which is made by Upjohn and which is a gelatin fortified compound. This gelatin compound is also further fortified with ephedrine and epinephrine to produce vasoconstriction and thereby to decrease further its rate of absorption. By so doing the effect may be prolonged to forty to forty-five hours. When Heparin is injected very little is found in the urine and practically none in the feces; therefore, most of it is destroyed in the body. Heparin is not toxic, except that it prevents the coagulation of blood and, therefore, is dangerous insofar as it may cause bleeding. The sodium salt of heparin in the aqueous solution (Upjohn) or Liquaemin Sodium (Organon) is available in various concentrations—10 mg. per cubic centimeter and 100 mg. per cubic centimeter are the most common methods of preparing it. These preparations are used for the intravenous route of administration. However, the 100 mg. per cubic centimeter concentration is suitable for the intramuscular route. The dose for the intravenous route, so-called intermittent intravenous medication, is 50 to 100 mg. of heparin every four to six hours. The continuous intravenous drip method which is used as a rule only when clotting time must be greatly prolonged is employed as follows: about 100 to 200 mg. of heparin are introduced in a liter of 5 per cent glucose solution in distilled water or in physiological saline solution. Usually 20 to 25 drops per minute are given. The intermittent intramuscular use of heparin in the aqueous solution is given approximately 1 mg. of heparin per pound of body weight initially and thereafter 0.5 to 0.7 mg. per pound of body weight every eight hours. The heparin sodium in the gelatin dextrose medium known as Depo-heparin sodium (Upjohn) is a product each cubic centimeter of which contains 200 mg. of heparin sodium. Four hundred milligrams of this drug are given, 200 mg. (that is, 1 c.c.) without vasoconstrictors and 200 mg. (1 c.c.) with vasoconstrictors. A dose of 400 mg. ordinarily produces a delay in clotting time for about forty-eight hours. When the drug is used by continuous intravenous drip the coagulation time must be determined at frequent intervals. It is desirable to determine it every eight to twelve hours. When it is given intramuscularly or when the fortified heparin solutions are used, it may be checked daily. Heparin is given subcutaneously so that if the absorption rate will be diminished, cold may be applied and thereby further aid in the vasoconstriction and prevent rapid absorption. It is recommended that it be given in the outer side of the thigh where blood vessels are sparse. If the coagulation time is too much prolonged, that is, more than thirty to forty minutes, it may be inactivated by the use of protamine, giving 1 c.c. for every 1 c.c. of heparin that has been used, or fresh blood transfusion may be employed. Following the use of aqueous heparin either intravenously or intramuscularly the coagulation time will return to normal in from two to eight

1. To curtail further bleeding:

Fall in blood pressure. This is the direct result of the loss in blood volume. Normally the blood pressure is due to the pumping action of the heart, peripheral resistance, and quantity of blood in the arterial system, viscosity of blood, and elasticity of the arterial walls. When the quantity of blood is reduced, the carotid sinus reflex causes vasoconstriction and cardio-acceleration. Perhaps the carotid body is stimulated also due to anoxemia which occurs. Marey's law states that the pulse rate is inversely related to the arterial pressure; that is, with a rise in blood pressure, it is slower and with a fall it is faster. This may occur by way of the aortic arch, afferent vagal, or by way of the sinus nerve.

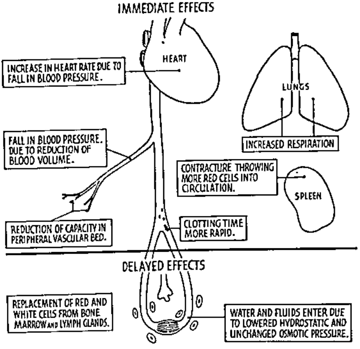

Fig 105.—Diagram illustrating the immediate and late effects of hemorrhage. The reduction of blood volume causes a fall in blood pressure. To compensate for this and to provide the vital centers with blood, peripheral vessels are constricted and the heart beats faster in an attempt to prevent a stagnant anoxia. The respiratory center is stimulated (due to cerebral anemia), and respirations are increased in rate and depth (air hunger). The clotting time decreases the fall in blood pressure, aiding this process. The spleen contracts, forcing more blood into the circulation. Fluid is drawn into the blood stream and after three to four hours causes great dilution. Replacement of cells is complete usually in a week. This varies with the amount of bleeding and the reaction of the patient's bone marrow

The Bainbridge reflex is described as an increase in heart rate caused by a rise in pressure of blood entering the right auricle. More will be said of these mechanics in Chapters 14, 17, and 18. However, the physiological effects rarely behave as single reactions but are multiple and complex The final result may be a temporary *increase* in blood pressure with a *slow pulse* early in hemorrhage. Later blood pressure falls but will rise again at short intervals. The fall in pressure is advantageous for it helps to curtail further bleeding. This is noteworthy during surgery

PHYSIOLOGICAL EFFECTS OF BLOOD LOSS

Blood and oxygen are absolutely essential to life. Deprivation of either constitutes the only real emergency. When more than 40 per cent of the blood volume is lost, the body is unable to repair the loss without the aid of transfusion, and the patient will usually die if this is not instituted. It is said that 500 c.c. of blood in a healthy adult will be replaced in an hour. Blood counts if made immediately after hemorrhage will be normal; soon, however, water is attracted to swell the depleted blood volume and the dilution makes the cell count and the hemoglobin concentration lower. Therefore, one cannot depend upon these counts for reliable information concerning the extent of the hemorrhage when they are made within one to two hours after severe bleeding.

When a man loses 500 c.c. of blood, he also loses 75 Gm. of hemoglobin and about 10 Gm. of plasma protein, or a total of 94 Gm. of protein if hemoglobin is taken as 100 per cent protein. Plasma protein may be regenerated at the rate of 1.3 to 11 Gm. per kilogram per day in the dog. If the same were true in a man weighing 60 kilograms he should be able to synthesize 78 to 660 Gm. of plasma protein a day, or the quivalent of 1,150 to 9,500 c.c. of plasma a day. Plasma proteins are not returned to the blood as fast as cells. The latter probably come from stores (spleen, some in liver and bone marrow). Protein is returned by way of the lymphatics from capillary filtrate and also by mobilization of proteins from depots (see Chapter 12). There is an increase in protein concentration in thoracic duct lymph following hemorrhage but not as much as after traumatic shock. It has been said that 20 per cent of the blood volume may be lost and it will be restored in seven to eight hours. Plasma protein will be slower to return. If thirty per cent is lost, shock usually develops, though not invariably. Shock slows up the process of blood volume restoration. Blood donors giving 500 c.c. of blood take about forty-three days to regenerate hemoglobin; this may be shortened by oral administration of iron.

The foregoing discussion illustrates how labile are the compensatory mechanisms and how unpredictable the effects of hemorrhage, when not massive. Even if blood is restored by transfusion, a patient may die if anemic anoxemia has so damaged capillaries and vital cells that irreversible changes are present. Thus the time element, the amount of blood lost, and the rapidity of its loss are important factors. More important is the ability of compensatory mechanisms to counterbalance the effects of hemorrhage. Let us now consider the early and later adjustments which occur.

Early Adjustments.—As a result of the loss of blood volume, physiological mechanisms attempt to curtail further bleeding, supply oxygen to the tissues, increase the blood volume by throwing in reserves, and contract the vascular bed to lessen the disproportion between circulating volume and vascular area, thereby avoiding shock.

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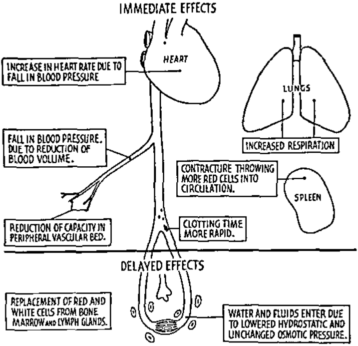

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for the arrest of hemorrhage due to trauma, or where the operation is accompanied by the loss of large amounts of blood. Small bleeders are often overlooked. Later, after operation, as blood and plasma are given, these may be troublesome, even dangerous. For this reason restoration of blood volume should be synchronous with its depletion. A persistent fall in blood pressure is the most reliable sign of concealed bleeding, although it should be stated that blood pressures as low as 30 systolic are tolerated for hours with recovery. This is not true in traumatic shock; and hemorrhage in patients with shock is disastrous.

Clotting of blood is favored by the lowered pressure and trauma at the site of injury, resulting in an increase in thromboplastin. Clotting time is more rapid in severe hemorrhage.

2. *To supply oxygen to the tissues:*

Increase in heart rate. This will be more fully discussed under the subject of shock (Chapter 14). Cardiac output is only slightly diminished after a loss of 500 c.c. of blood but is greatly diminished after the loss of a liter and during syncopal attacks as determined by the ballistocardiograms. The acceleration of pulse may not occur after hemorrhage with a patient lying quietly but should he move about or try to rise, it becomes rapid and the blood pressure falls. Usually a rapid pulse is an early sign in concealed hemorrhage and is brought about through carotid sinus and aortic reflexes which are initiated by the fall in blood pressure. This is an attempt by nature to increase the rate of blood flow to compensate for the blood's diminished oxygen-carrying power. It is noteworthy that during the syncopal attacks there may be a bradycardia which occurs with vasoconstriction; this is transient and with signs of collapse comes the rapid pulse rate.

Increased respiration is designed to relieve the anemic anoxemia. It is caused by the anoxia of the chemoreceptors of the aortic and carotid bodies which are deprived of sufficient oxygn due to diminished blood flow. At first there is an increase in the rate and depth of breathing; later, if the hemorrhage is profound, sighing respiration occurs (air hunger); still later this may become Cheyne-Stokes in type, gasping respirations just before death.

3. To increase the circulating blood volume and decrease the disproportion between the diminished blood volume and the size of the vascular bed:

Contraction of the spleen which is a huge reservoir for red blood cells produces an erythremia. Webster showed the restorative possibilities of the spleen by means of its hidden resources of blood cells which he excluded by preliminary removal of that organ. Some evidence of the source of part of the restorative fluid was discovered by excluding certain viscera from the circulation. In their absence the rate of blood dilution was greatly diminished. There are observations to support the belief that even in man the immediate rate of entrance of fluid into the

blood stream after hemorrhage may amount, for a time, to 0.25 c.c. per kilogram of body weight in a minute.

Reduction in capacity of the vascular bed occurs and there results a redistribution of the blood. This is accomplished by vasoconstriction which is known as the "physiological tourniquet." By this method blood is withdrawn from the less important parts and organs and is given to the more vital ones. The pallor of the skin and mucous membranes and the coldness of the body is a part of the phenomenon of shock, in this instance due to loss of blood. It is a conservative dynamic mechanism designed to prevent irreversible shock in which instance there is peripheral vascular failure. The skin, then, becomes mottled and cyanotic in places. Pressure causes a blanching of the skin which returns to its previous color very slowly.

Adolph has summarized the further *immediate effects* of hemorrhage as follows: the primary effect of loss of blood from the circulation is to *decrease the rate of blood flow and oxygen flow to most tissues.* To this situation the circulation responds by increase in heart rate, discharge of epinephrine, discharge of blood from the spleen, local vasoconstrictions, and local persisting ischemias. The respiration responds to the local asphyxia in its centers and to the pouring of lactate into the circulation by hyperventilation (dyspnea and "air hunger"), followed eventually by anoxemia and cessation of breathing.

Hemodilution attempts to restore blood volume. This begins immediately after hemorrhage and is due to the lowered hydrostatic and unchanged osmotic pressure of the blood which causes water to be drawn in from the tissue spaces (Chapter 11). In the capillaries, fluid flows into the blood from the tissue spaces, water excretion by the kidneys is diminished, and various dissolved constituents interchange in response to the lowered pressures, to the anoxemia, and to the altered types of tissue metabolism. After several hours the blood becomes diluted and therefore the red cell concentration is reduced. This constitutes the most reliable means of differentiating hemorrhage from shock; in shock, plasma is lost so that the red cell concentration is increased. This hemoconcentration in shock begins within one-half hour; in hemorrhage, dilution may be detected within two hours, although it is sometimes greatly delayed, especially in dehydration. Later, after the blood volume has been restored, protein is added to the blood by way of the lymphatics, which are found to contain more protein, for there is a greater concentration of protein in the intercellular fluid. This is due to increased capillary permeability from anoxemia. Intercellular fluid enters by absorption through the blood capillaries. The extreme thirst of the patient after hemorrhage is easily understood, for the tissue cells have been depleted of their fluid content.

If the capillaries have been injured, as in crushing wounds, or if the hemorrhage is great and prolonged, or if there is dehydration, capillaries

become permeable to colloids (in the former case due to direct injury and in the latter due to anoxemia). This permits loss of plasma and results in a high hematocrit reading. Some fluid is attracted into the blood stream and is promptly lost again with more plasma, thereby producing hematogenic shock (see Chapter 14). In dehydration there is very little intercellular fluid to draw upon and therefore shock which is irreversible may soon occur. Thus hemoconcentration may be present and persist in hemorrhage. Usually there is a normal hematocrit early, then a low one. The observation that shock due to trauma begins with hemoconcentration whereas shock due to hemorrhage ends with hemoconcentration is ordinarily, although not invariably, correct. The reasons for this phenomenon have usually been explained by the increased permeability of the capillaries. In shock they leak early due to trauma; in hemorrhage late due to anemic anoxemia. Fluid is also lost in both instances by rapid respiration and leaky skin. Recent experiments tend to disprove the hypothesis of leaky capillaries as a cause of irreversible shock in hemorrhage—rather it is due to permanent injury of tissue cells from anoxemia and dehydration. Probably both factors are responsible. However, it is important to remember that transfusions are often restorative in shock due to hemorrhage, even after many hours. This is not true in traumatic shock. Ultimately, though, shock due to hemorrhage is also irreversible.

Replacement of the red and white cells and protein.—This is done by the blood-forming organs and takes several days or weeks. The liver is usually not damaged in hemorrhage. Bone marrow is stimulated by the anoxemia in hemorrhage. The reason for this is that the most important factor in erythropoiesis is the oxygen tension in bone marrow. Conversely blood transfusion depresses it as does the inhalation of oxygen.

CAUSES OF BLOOD LOSS AND KINDS OF BLEEDING

Bleeding may occur from the arteries, the veins, or the capillaries. It may be internal, external, or concealed and may be primary or secondary. Arterial bleeding may be identified by the bright red color, the force, and the spurting tendency. A lateral tear in an artery bleeds more than a transverse one due to separation of the wound by contraction of the circular muscle in the media. Venous bleeding is darker, and although it may have considerable force, it does not approach that of arterial and does not spurt. Capillary bleeding is an ooze and its color depends upon whether there is a predominance of venules or arterioles in the wound. While it is true that in most cases of hemorrhage due to accidents both veins and arteries are involved, yet it is necesssary to distinguish between them, especially if one or the other is injured alone.

When hemorrhage occurs from certain organs, special names are applied: *epistaxis* refers to bleeding from the nose; *hematemesis*, to bleeding from the stomach; *hemoptysis*, to bleeding from the lungs; *menor-*

rhagia, to profuse or abnormal bleeding from the uterus at menstrual time; and *metrorrhagia*, to bleeding between periods. It is probably well to drop these terms and speak of gastric hemorrhage, pulmonary hemorrhage, etc.

External hemorrhage and internal hemorrhage are what the names imply. The former occurs on the outside and can easily be seen. The latter occurs within the abdomen or thorax, or within one of the parenchymatous organs such as the liver, spleen, or one of the kidneys. Concealed hemorrhage is a term used to indicate bleeding into muscle or beneath the skin. This is very important in accidents and usually causes a profound state of shock (Chapter 14).

Immediate hemorrhage means one that occurs at the time of operation. Delayed or secondary hemorrhage usually refers to bleeding which occurs after forty-eight hours as a result of a slipped ligature or infection about a vessel which causes the clot to become loose.

SYMPTOMS AND SIGNS OF HEMORRHAGE AND THE DETERMINATION OF THE AMOUNT OF BLOOD LOST

The symptoms accompanying hemorrhage may be said to depend on the amount and rapidity of the bleeding. Small hemorrhages produce few or no immediate symptoms, unless because of the psychic effect simple fainting occurs. Large hemorrhages produce symptoms of shock. If the hemorrhage is small in amount and continued over a long period, a profound state of anemia occurs. A sudden large hemorrhage produces shock, but the patient may quickly rally, especially if the bleeding is controlled. However, if a large volume of plasma has been lost, symptoms may persist in an alarming way even after the arrest of the hemorrhage. *In both instances there is a loss of blood volume followed by cardiac inadequacy and a fall in blood pressure.* The patient appears pale, the lips are blanched, and the skin is moist and cold. *He is extremely restless.* The temperature is below normal, the pulse is rapid and thready, and the respiration is rapid and shallow, or sighing. The patient complains of being unable "to get his breath" and of weakness and thirst. The restlessness is a compensatory mechanism to increase venous return through muscular contraction. Patients after a severe hemorrhage desire to be propped up in bed, or to lean forward, hoping to alleviate the dyspnea. These symptoms may ameliorate when the "compensatory mechanism" takes hold, only to revert back into more severe ones as the bleeding progresses. Hence the patient is said to have a succession of fainting spells.

In concealed hemorrhage, where bleeding is slow but continuous due to capillary damage, profound shock occurs (Chapter 14). Whereas the foregoing symptoms are those of the typical case, many variations occur. We have already noted that the pulse may be slow and the blood

become permeable to colloids (in the former case due to direct injury and in the latter due to anoxemia). This permits loss of plasma and results in a high hematocrit reading. Some fluid is attracted into the blood stream and is promptly lost again with more plasma, thereby producing hematogenic shock (see Chapter 14). In dehydration there is very little intercellular fluid to draw upon and therefore shock which is irreversible may soon occur. Thus hemoconcentration may be present and persist in hemorrhage. Usually there is a normal hematocrit early, then a low one. The observation that shock due to trauma begins with hemoconcentration whereas shock due to hemorrhage ends with hemoconcentration is ordinarily, although not invariably, correct. The reasons for this phenomenon have usually been explained by the increased permeability of the capillaries. In shock they leak early due to trauma; in hemorrhage late due to anemic anoxemia. Fluid is also lost in both instances by rapid respiration and leaky skin. Recent experiments tend to disprove the hypothesis of leaky capillaries as a cause of irreversible shock in hemorrhage—rather it is due to permanent injury of tissue cells from anoxemia and dehydration. Probably both factors are responsible. However, it is important to remember that transfusions are often restorative in shock due to hemorrhage, even after many hours. This is not true in traumatic shock. Ultimately, though, shock due to hemorrhage is also irreversible.

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Should bleeding persist, operation is indicated, especially in older patients, who stand the loss of blood poorly. Of course, it would be better to wait until the patient had recovered from the hemorrhage—many patients are lost by overconservatism. Younger ulcer victims will usually recover from the first hemorrhage but even here a recurrence demands surgery. (See Chapter 20.)

Bullet wounds of the abdomen or severe trauma are followed by recovery almost in proportion to the amount of bleeding encountered and the time interval before intervention. There is only one way to control prodigious internal bleeding from trauma and that is by open operation with ligation or suture of the bleeding part. If this ligation impairs the blood supply of an organ, the organ must be removed. Since patients with large hemorrhages are usually in shock, this is combated by adequate replacement of blood immediately before and during the operation. Two large veins, preferably in the ankle, are cannulized and blood plasma and saline are infused. If upon opening the abdomen massive hemorrhage is encountered, blood may be given almost as fast as it is lost. Another devise may be added for safety. Should the blood pressure fall to such levels that cardiac inadequacy prevails precluding the rapid ingress of blood, the vital fluid may be forced into the veins by an attached 50 c.c. syringe with a three-way stopcock. In intra-abdominal bleeding the course of the bullet is traced. What organs were in its path? What vessels are likely to be torn? Incision is made which is adequate. These vessels are seized and tied; if a solid organ is torn, the rent is packed with gauze until the extent is estimated and sutures can be introduced. In combined thoracic and abdominal wounds the same procedure is followed. A typical example of this problem may be cited.

A young soldier who had just returned from Germany was dismantling a 38-caliber revolver. He shot himself in the fifth interspace just to the right of the sternum and the bullet emerged below the twelfth rib in the loin. He was in profound shock. The right chest was dull, the abdomen tense, and the urine bloody. His blood was typed and 3,000 c.c. of plasma were given, which was followed during surgery with 1,500 c.c. of whole blood. Incision was made in the ninth intercostal space posterolaterally. The internal mammary artery was tied at both ends. Two large holes in the upper and lower lobes of the lung were sutured. The diaphragm was opened and the liver found to be badly torn. It was packed temporarily and the retroperitoneal space opened. The right renal vein had been severed and the kidney badly torn. Right nephrectomy was done and the liver was sutured. The patient made a quick recovery. This story probably was duplicated in World War II thousands of times.

Ligation.—The ideal way to arrest bleeding from a vessel is by ligation. Some have advocated the simultaneous ligation of artery and vein where large vessels to an extremity are involved in order to prevent gangrene. Ligation of the concomitant vein is said to increase the venous pressure and thereby cause a dilatation of the venules which in turn is transmitted into the arterioles; thus there develops a more ample collateral circulation than might otherwise have occurred. Experimental and clinical studies have not substantiated this claim.

pressure normal. These are transient episodes as a rule and are not seen in severe cases after a variable interval. *It is this interval which is apt to deceive the surgeon during and after surgery.* Blood loss cannot be determined early by clinical symptoms or signs or by the hematocrit, hemoglobin, or plasma protein determinations. After the patient reaches a point where compensatory mechanisms no longer prevail, sudden and dramatic shock may occur. This often happens near the end of the operation or soon after the patient is returned to his room. Shock may not occur at all, *yet a blood loss of 500 to 750 c.c. may retard recovery. It* is, therefore, desirable to know the amount of blood lost during an operation, so that it may be replaced. Blood loss has been ascertained by washing sponges, drapes, and gloves, measuring the quantity in the aspirating bottle, and then testing the hemoglobin. Since the preoperative hemoglobin is known, then the $\frac{\text{Hgb lost}}{\text{Hgb preoperative}} \times 100 = $ c.c. blood lost.

Another method is to use dry sponges of known weight and weigh them as they are discarded. In this way blood may be given as it is being lost. Our method is based upon an estimation of the amount of blood usually lost in the particular kind of procedure and then commensurate replacement as the operation progresses. Should there be an unusual amount of bleeding, the amount is increased. The amount of blood lost *may be small, but in children or light patients it may mean a large per* cent of body weight and must be replaced. Our method is admittedly inaccurate but will prevent sudden collapse during the symptomless periods of hemorrhage.

METHODS OF CONTROL OF HEMORRHAGE

Natural Arrest.—Nature may stop a hemorrhage without surgical aid and frequently does so. This is accomplished by clotting, *retraction* and contraction of the vessel wall, and lowered blood pressure, which not only favors clotting, but allows the clot to begin its organization. Anything which interferes with the organization of the clot prolongs bleeding. Without clot formation and organization, hemorrhage is not arrested, even though the vessel be ligatured or sutured. Scalp vessels are held in the tight subcutaneous layer and cannot retract and contract well; *therefore bleeding from scalp wounds is profuse.* An example of the management of hemorrhage is the treatment of bleeding from a gastric ulcer. This consists of rest to the part (a limited amount of water, bland food, small doses of alkalis to neutralize the irritant action of the hydrochloric acid), absolute rest for the patient (through ample doses of morphine), and small and repeated *blood transfusions (not enough* greatly to increase the hydrostatic pressure, yet enough definitely to *increase* the osmotic pull). The introduction of large quantities of fluid intravenously may raise the blood pressure and lower the osmotic pull sufficiently to release clots and cause more hemorrhage.

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Concussion of an artery leads to spasm with absent pulsation which may be misleading. When a ligature is applied, intima should be in contact with intima. This contact should be broader in large vessels (that is, the ligature should be larger) and narrower in smaller vessels. The trauma to the intima stimulates clotting. (The ligature should not be so tight as to cut through the vessels.) The circular muscle fibers in the media contract, constricting the lumen further. Soon fibroblasts, fibrocytes, macrophages, and leucocytes appear on the fibrin within the clot. (The fibroblasts come from the adventitia.) Collagen forms and hardens, debris is removed by the macrophages, and the endothelium proliferates to cover the site of the ligature, making the vessel smooth. It is well to transfix the ligature and leave a cuff of about one-eighth inch so that it will not be forced off the end of the vessel.

Heavy silk or cotton is preferable to catgut for ligature because it is more pliable and has a greater coefficient of resistance so that knots do not slip. For largest vessels umbilical tape has been advocated by some.

A partial division of a vessel or a lateral tear may bleed more profusely than a complete transection, due to contraction of the circular muscle in the tunica media, which further opens the wound. Frequently a "false aneurysm," or large hematoma, may form. In such cases ligation proximally and distally must be done and the sac obliterated. Indeed, both sides of a divided artery must always be tied, for bleeding will occur both proximally and distally to the wound, due to collateral circulation. This is especially true in the larger arteries and such smaller vessels as the internal mammary and deep epigastric. Ligation and division of large arteries is preferable to ligation in continuity because in the latter there may be erosion and hemorrhage or reestablishment of lumen; also, years later such a procedure may be followed by pain, poor pulse, and claudication. Should this occur even division of so little as a fibrous cord relieves pain. When the artery is divided, the retracted, thickened, and expansile end obviates the above. Badly mangled vessels bleed very little because the trauma injures the intima and the injury stimulates clotting. Thrombi form which cause the arrest of hemorrhage in the smaller vessels and often, temporarily, in the large ones. Thrombosed arteries do not lend themselves to primary suture. These thrombi may give rise to emboli. If badly contused, ligation above and below and excision of the thrombosed area should be done. Suturing is disappointing because of thrombosis. Even if successful, aneurysmal dilatation may follow or there may be severe pain and disuse of the extremity with atrophy. In some instances, if the wound is an incised one (and is lateral or involving part of the circumference) and if the patient is seen within six hours so that complete sterilization can be effected, suture of the vessels may be attempted. It is best to use fine, waxed silk for this, and intima should be approximated to intima if possible. How-

ever, until the ligature can be used, temporary means of stopping the hemorrhage must be employed. Perhaps the best is the tourniquet. Anything may be used—a handkerchief may be twisted or a catheter may be tied tightly. Although experiments to the contrary have been reported, we have found a wide rubber bandage such as the Esmarch band *or blood pressure cuff is best.*

Temporary Control by Tourniquets.—By consulting the diagrams an idea may be obtained as to the more advantageous sites for applying tourniquets. It should be noted that the tourniquet is applied where the vessel is in immediate contact with bone and can be compressed against it. In the arm this would be above the elbow, and in the leg, above the knee, compressing the brachial artery and the femoral artery, respectively.

Although this point of compression stops the hemorrhage most effectively, yet it should be borne in mind that the radial nerve in the arm and the sciatic nerve in the leg demand a broad elastic tourniquet to *avoid injury to these structures if the tourniquet must remain in position* for a considerable length of time. The elbow joint and knee joint areas should never be used for tourniquets because of the danger of injuring vesicles and nerves, particularly the common peroneal. The forearm and lower leg may have any type of tourniquet.

The tourniquet may be left in place up to four hours if it is of the broad elastic type. The five factors which limit the period of safety are *gangrene, injury to the nerves, trauma to the skin, decrease in tissue* resistance by anoxia, and shock on removal of the tourniquet.

Experimental and clinical evidence show that a tourniquet may be left on longer when the extremity is packed in ice. This procedure is unnecessary as a rule and may lead to gangrene as a result of the cold. (See Chapter 6.) The tourniquet may be released temporarily to facilitate reoxygenation. During this time bleeding may be controlled by digital pressure and elevation of the extremity. If this is impossible the tourniquet must be left in place. We shall discuss the effect on the blood pressure after release of the tourniquet in Chapter 14. It is pertinent to recall that all preparation should be made for attention to the wound when the tourniquet is released and blood transfusion should be in progress. This may prevent a severe state of shock. It is better to apply an elastic pressure bandage with control of bleeding than to use the tourniquet to control bleeding. In every instance the extremity should be elevated for a few minutes before applying the pressure bandage. These measures are designed to prevent the sudden pooling of blood into the injured extremity following the release of the tourniquet, whether this pooling is due to paralysis of vessel walls or vasodilation. Local axonal nerve reflexes with dilatation of the capillaries, or dilatation due to local tissue histamine-like substances or due to an increased acidity of tissues, all play a role in the production of so-called tourniquet shock.

From this discussion it is obvious that in contemplating surgery, tourniquets are not often employed. In such cases the blood supply is controlled first by ligatures. It is in traumatic surgery, as well as in vascular surgery, that tourniquets are employed, and here the limitations in such procedures should be fully understood. (See Chapter 17).

Needless to say, the tourniquet must be applied between the heart and the site of hemorrhage. In the neck, pressure is applied on the carotid artery by compressing it against the carotid tubercle. It has been said that a broad band used as a tourniquet will cause more damage to the vessel than a narrow one, because of a wider area of compression

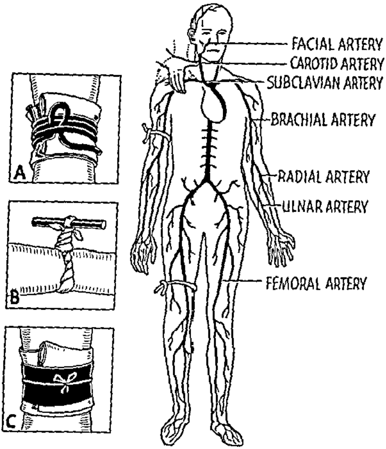

Fig. 106.—Diagram illustrating types of tourniquet and places of application. *A.* Soft rubber tube wrapped around a towel. *B.* Handkerchief tied around a stick and twisted. *C.* Esmarch bandage—the ideal type of tourniquet for the control of hemorrhage.

The large figure indicates the proper sites for the application of the tourniquet. It should be above the elbow and knee where the main vessels can be compressed against the underlying bone. The hand indicates the sites of pressure in the event of bleeding from the common carotid, which has no branches, except its terminals (the external and internal carotids). Pressure is applied medially against the cervical spine. The dotted hand indicates the direction of pressure in hemorrhage from the subclavian artery. Obviously, pressure is made proximal to the wound in the vessel—that is, between the injury and the heart. Venous bleeding may be controlled by pressure at the site of hemorrhage.

injury. This may be true, but our experience has been that narrow bands left on for two hours or more are more apt to produce a paralysis due to nerve injury or gangrene due to arterial and venous damage. It is true that if an extremity is packed in ice and the temperature m

at about 5° C. a tourniquet may remain for seven to ten hours without resultant gangrene. This is useful where transportation over a long distance is necessary. Usually, however, gangrene supervenes after such treatment and amputation is necessary.

Pressure for the Control of Hemorrhage.—Venous bleeding is best stopped by using pressure at the site of hemorrhage. The vein has thin walls which are readily compressed, and it is unnecessary to use a tourniquet. To be effective, a tourniquet must be tight enough to occlude the arterial flow: Should the pressure applied by tourniquet be less than systolic, it would only increase the venous bleeding. Tourniquets applied below the site of hemorrhage in venous bleeding also tend to increase it, due to collateral communication.

It may be said that pressure at the site of bleeding may be used in any type of hemorrhage, and, if firm enough, will be effective. In the case of a large bleeder, the finger may be used until a tourniquet can be applied. Every surgeon has encountered severe bleeding during an operation. Until he can apply a hemostat he will invariably control the flow of blood with the fingers. Capillary oozing is best arrested by pressure. This is applied usually by gauze packing and is especially useful in bleeding from the nose, from a tooth socket, from the cervix, or from the uterus. Packing should be left in long enough for clotting to occur and, if possible, for a sufficient exudate to form to loosen the packing. This may be twenty-four to forty-eight hours, or even longer. If simple pressure is applied to capillary ooze on the surface, one must remember that at least four to six minutes are necessary to effect clotting. In the case of a mangled extremity, the bleeding is usually concealed, and a tight elastic bandage over a previously applied sterile bandage controls capillary as well as arterial bleeding most effectively and with the least amount of shock after its release.

Local Coagulants and Hemostatics.—Styptics, such as 10 per cent silver nitrate or glacial acetic acid, are sometimes used in the nose or throat effectively. The escharotic action of these solutions predisposes the area to recurrent bleeding. A piece of skeletal muscle held with pressure is often effective. Fibrin foam prepared from human fibrinogen and thrombin is now available in sterile tubes. The film is soaked in physiological saline and then removed and kept in cool saline. It has been left in place as a dural substitute and has also been used over raw surfaces in the abdomen. Topical thrombin is excellent, producing coagulation in a few minutes. The gelatin sponge may be left in place producing hemostasis and ultimately being absorbed with fibrous tissue replacement. Oxidized cellulose or cellulosic acid (absorbable gauze) is also effective but is absorbed more slowly and causes more adhesions to form. It cannot be used with topical thrombin because its acid reaction inactivates thrombin, whereas if alkaline solutions are used, the gauze is ineffective.

Agents Used to Increase Coagulability of the Blood.—Human plasma is perhaps the most effective substance to increase blood coagulability. Whole blood should also be used because the agglutination of platelets and erythrocytes is the starting point of thrombus formation; therefore they must be present in ample quantity. Since abnormal bleeding tendencies have already been discussed, we need only recall that the following deficiencies may be present: thromboplastin, for which whole blood and plasma is necesssary; prothrombin, for which vitamin K is essential; fibrinogen, which is most effectively treated by plasma and blood transfusions; calcium may be used because of its indirect action on the liver; erythroblastosis is perhaps best treated with Rh-negative blood.

Dozens of commercial products are available which are supposed to accelerate blood coagulation. Most of them are inert. Oxalic acid is apparently an effective hemostatic agent. Under the heading of anticoagulants we have stated that sodium, potassium, or magnesium oxalate will prevent clotting in vitro. Calcium oxalate is formed, causing calcium depletion and prolonged clotting time even in vivo and if given in excessive amounts will cause death of the animal. However, when given in small amounts, coagulation time is reduced even in hirudinized animals, indicating that here it is antagonistic to antithrombin. The normal person has about 5.5 to 7.5 mg. of oxalic acid per 100 c.c. of blood. Oxalemia accompanies hyperglycemia and perhaps this is the reason for reduced coagulation time produced by the administration of glucose or adrenalin. Oxalic acid given intramuscularly in 20 mg. doses may help in the control of capillary bleeding due to prolonged coagulation time.

I have on two occasions operated upon physicians, who had hemophilia. In one, who was a resident in medicine, the coagulation time was thirty-two minutes. He had an acute appendicitis which at operation was found to be gangrenous. The second was an intern with a strangulated inguinal hernia. His clotting time was twenty-nine minutes. In both, 1,000 c.c. of plasma were given before and during surgery. Meticulous hemostasis was observed. Both recovered without any bleeding episodes. In both cases procrastination was untenable. Both knew that they had hemophilia. These cases are cited to prove that perhaps the major portion of postoperative bleeding is due to inadequate attention to the smaller vessels which should be tied.

REPLACEMENT OF BLOOD

After the temporary arrest of the hemorrhage treatment is directed to the patient as a whole, for he will usually be in a state of shock and operations should not be done with a patient in shock even though they are apparently minor. A good rule to follow is: arrest hemorrhage first and then treat the patient for shock. After reaction has occurred, attention should be given to the wounds.

Experiments have shown that an amputation may be done successfully *with hemoglobin values as low as 28 per cent.* Surgeons regard a hemoglobin value of 50 per cent as the lower limit of safety as a rule. The limit varies, of course, with the general condition of the patient.

This means that a patient in shock will not tolerate the loss of blood even though it be trivial. Furthermore, we have seen that hemoglobin and erythrocyte values may be normal for several hours after a severe hemorrhage, thus misleading the surgeon.

Obviously the first consideration will be the replacement of blood. For this, fresh whole blood is best. Patients with continued blood loss and continual replacement are bad risks even though blood counts and hemoglobin are within normal limits. This is due to the severe crippling changes which occur in tissue cells as a result of continual anemic anoxemia. Surgical wounds heal poorly and renal or hepatic insufficiency is apt to occur. These observations are often seen in bleeding peptic ulcer. Here surgery should be done early for persistent hemorrhage (forty-eight hours), and if not we should wait for spontaneous arrest. Should surgery become mandatory, the simplest procedure possible is done.

Whole Blood

A fundamental rule in restoring blood volume is to replace that which which has been lost. In hemorrhage it is whole blood. Later we shall discuss substitutes, but first we should enumerate the reasons for giving whole blood, then outline the differences between fresh and stored blood, and finally list the reactions from blood transfusions.

Whole blood may be given in any condition in which there has been a decrease in circulating blood volume from any cause, including the loss of plasma and electrolytes in burns. The transport of oxygen by the red cells, the maintenance of osmotic pressure by the plasma proteins, the coagulation of blood through the prothrombin-fibrinogen mechanism, nutrition as supplied by plasma proteins, participation in immunity reactions through complement and circulating antibodies, and phagocytosis by the leucocytes are all functions of whole blood, making it the fluid best suited to fortify the circulation. Patients tolerate a slow loss of blood well, but when red cells are suddenly removed in large numbers, an anemic anoxemia results which can only be met by introducing red cells (even the inhalation of 100 per cent oxygen will not help if there are not enough cells to carry it). Pure crystalline human hemoglobin may be made from discarded red cells in blood banks. This is still in the experimental stage.

Giving fresh blood means careful typing and compatibility tests, Rh factor determination, especially in women, and the availability of compatible donors. While this is ideal it is as a rule impractical and therefore most hospitals have blood banks from which compatible stored blood may be had at all times. Blood transfusions are almost uniformly

given by the indirect citrate method. This is simple and efficient. Blood is drawn from the donor in a vacuum bottle in which there is a solution of sodium citrate. It is typed and used or stored. Stored blood is kept at 2 to 4° C. for ten days but no longer because hemolysis takes place in increasing amounts. After ten days the plasma is removed and may be used (care being taken to leave the buffy coat and hemolyzed cell layer because these cause reactions). This plasma may then be dried, frozen, or kept in a liquid state in refrigeration. Stored blood has other disadvantages:

1. By using radioactive iron, donor red blood cells can be labeled. The storage of citrated blood exerts a deleterious effect on the survival of transfused erythrocytes. Their survival varies inversely with the duration of storage. The iron of destroyed transfused erythrocytes is utilized for the synthesis of hemoglobin.

2. The potassium content of whole blood is greatly increased even without hemolysis; at the end of one week it may reach five to ten times the normal amount. Hyperpotassemia may cause convulsions or cardiac effects.

3. Prothrombin content is depressed up to 25 per cent by the end of seven days.

4. Electrophoretic patterns indicate certain alterations in proteins, but their significance is not definitely known.

5. The antibody effect is less, even though the globulin content is normal.

6. Leucocytes are decreased 50 per cent after five days of storage. Moreover, the remaining white corpuscles lose some of their phagocytic powers.

7. Platelets survive only two to five days.

We have stated that the indirect method is by far the more practical; however, the dangers of excessive amounts of citrated blood given within a very short period should be mentioned. Severe toxic reactions may occur from the sodium citrate. This may be due to its effect on heart muscle or its ability to shorten clotting time due to destruction of platelets, with resulting thrombi; it may form a complex salt with calcium and remove it—this, as we have seen, prevents clotting in vitro and may produce tetany in vivo.

As little as 0.11 to 0.15 Gm. of sodium citrate per kilogram of body weight may be lethal when given in plasma or blood. Therefore 2,500 to 3,500 c.c. of blood or plasma given rapidly to a person weighing 70 kilograms may be toxic (since 10 c.c. or a 2.5 per cent solution of sodium citrate is used for every 100 c.c. of blood), although we have never recognized this phenomenon in our patients thus far.

Reactions from blood transfusions may also occur due to pyrogenic substances in glassware or tubing, imperfect technique, too rapid injection, or too much blood, especially in children. In the latter there may

result an embarrassment to the right side of the heart. The quantity is about 20 to 30 c.c. per kilogram of body weight or 10 to 15 c.c. per pound or about 25 to 30 per cent of the total blood volume; however, this varies with the amount lost which should be adequately replaced. In adults *larger amounts may be given up to 45 c.c. per kilogram or 50 per cent* total blood volume. It is usually better to replace blood slowly after control of hemorrhage because diluting mechanisms may have already replaced part of blood volume temporarily. Incompatibilities may cause severe, even fatal reactions. Symptoms include precordial pain, which may be referred "straight through" to the back, tingling pains all over the body, cyanosis, and all signs of shock. Hemoglobin appears in the urine. Symptoms are due to the mechanical effect of agglutinated corpuscles, causing a blockage of vessels to vital organs. Hemolysis of agglutinated cells occurs late. The tubules of the kidneys are blocked with hematin produced by the action of the acid urine on the liberated hemoglobin. This may cause anuria. Reactions may also occur due to the ingestion of protein or other food by the donor—these may resemble anaphylaxis or serum sickness. Intragroup reactions may be due to the Rh factor or isoimmunization with the A and possibly B antigen in mothers.

Treatment of Transfusion Reactions.—For any type of reaction the *transfusion should be stopped at once. In the less severe, a change of* tubing may be all that is necessary. In the severe types due to incompatibility, active treatment is required in addition to stopping of the transfusion. This consists of giving plasma if necessary as a substitute, giving large doses of sodium bicarbonate by mouth if possible (if not, intravenously) to alkalinize the urine; also a 1/6 molar sodium lactate solution may be used intravenously if the patient cannot swallow. Beware of overhydration in anuria due to transfusion reaction; however, extra sodium which is needed in hemoconcentration and acidosis must be supplied with physiological saline solution. Osmotic pressures may be sustained with plasma.

Substitutes for Whole Blood

Plasma.—When blood stands, plasma and serum form on top. Serum contains no fibrinogen. Plasma is preferable to serum because the latter contains substances which exert vasomotor effects and there are other unfavorable reactions. Plasma may be preserved in liquid, frozen, or dried state. In civilian use liquid or frozen plasma is best, although the former offers the least resistance to bacterial growth. Dried plasma losses prothrombin when diluted with sterile, distilled water. If 0.1 per cent citric acid solution is used, excessive alkalinity may be avoided and much prothrombin saved. Hypertonic solutions of the dried plasma should not be used; unlike iso-osmotic solutions they depend on the

intercellular fluid for their dilution. Since dehydration is apt to be present and since tissue water is being used to keep up blood volume, iso-osmotic plasma is best.

Albumin solutions may be used and are available. They are best suited for the treatment of shock in military campaigns. Since the albumin fraction is the most important in maintaining osmotic pressures, this solution is useful, but if given in hypertonic solution it is objectionable for reasons given.

In general, plasma is useful to avert shock from hemorrhage. A patient already in shock stands the loss of blood poorly. Shock due to hemorrhage begins abruptly when compensatory mechanisms fail (q.v.). Here plasma restores blood volume, keeps up osmotic pressure, provides a normal medium for carrying all available red cells, and serves to mobilize sequestrated erythrocytes, actually increasing the number of circulating red corpuscles. Since the corpuscles increase in size after a hemorrhage, they are thought to be trapped in smaller vessels and are freed after plasma infusions restore normal osmotic and volume relations.

Red Blood Cells.—They may be given in physiological saline. This is impractical ordinarily. However, during World War II plasma was used and the cells discarded because in the earlier years of the conflict a satisfactory method for preserving whole blood for long periods had not been found. These cells were available in all blood donor centers and were used in treating hemorrhage. There were more reactions than with whole blood, and the cells could not be kept for more than seven to ten days.

Human Fluids.—Pleural fluid and ascitic fluid have been used and show promise of being useful if they can be given without serious reactions.

Other Proteins.—These have been discussed in the previous chapters. Amino acids and hydrolyzed protein are not useful as blood substitutes and may not be used even as a temporary measure in hemorrhagic shock. Gelatin has been tried but is apt to be followed by reactions.

Plant Derivatives.—Plant derivatives such as acacia and pectin while able to exert effective osmotic pressures are inert, interfere with oxygen absorption by the red cells, and impair the function of the liver and other parenchymatous organs. They also cause pseudoagglutination.

Crystalloids.—Physiological saline or isotonic (5 per cent) glucose solutions or combinations may save lives. Although their action is temporary for reasons already discussed (Chapters 11 and 12), they are able to bolster blood volume and supply the tissues with water and sodium. They are always available and are tolerated safely. Furthermore, they are useful to precede and follow transfusions of whole blood or plasma.

After reaction from hemorrhagic shock which is sufficient to permit definitive treatment, operations of necessity are performed. The pa-

tient is placed in an environmental temperature of about 72° F. and is carefully watched for secondary hemorrhage which may occur upon the return of a normal blood pressure. Pulse and blood pressure readings are made at one-half-hour intervals. Rectal temperatures are taken every three hours. A record is kept of fluid intake and output. In addition, hematocrit and plasma protein determinations (by copper sulfate method) are made every twenty-four hours to follow blood and plasma regeneration. Red blood counts and hemoglobin readings may be used as a supplement or in place of hematocrits if this method is not available. Thus the amount and type of fluid is given which is needed to restore normal values. As a rule very little is needed after the initial restoration of blood volume if the hemorrhage has been controlled.

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Chapter 14
SHOCK

Shock is a term that is difficult to define because when used categorically it embraces such a vast array of disturbances that it is practically meaningless. Indeed an attempt to describe it leads to a recitation of so many variations in the clinical manifestations, causes, laboratory studies, and primary and secondary physiological effects that many have urged a discontinuance of the use of the term. Since the word is in common use it is well that we attempt to define it and then discuss the subject within the confines of the definition.

Shock is not a disease entity but a dynamic syndrome brought on by a general injury to the organism from nervous, mechanical, chemical, bacterial, or traumatic causes. Its symptoms are due to the failure of compensatory mechanisms to adjust to a sudden greatly diminished (rarely increased) *circulating* blood volume. Thus there are three principal reasons for shock: (1) a loss of blood volume so great that decreased adjustment of the vascular bed cannot occur; (2) an increase in volume so great that the vascular tree cannot increase enough; (3) a failure of adjustment due to (a) nervous or (b) organic change in the blood vessels. The symptoms of shock then are really the manifestations of the compensatory mechanisms in charge when the disproportion became too great for the maintenance of normalcy. Each symptom thus becomes an act of conservation designed to preserve the integrity of cells in such vital organs as the brain, heart and blood vessels, liver, kidneys, and lungs, for if such cells are irreparably damaged, then shock becomes irreversible and the individual will die even though restorative measures have been instituted.

Let us look at a patient who presents what has been termed the classical picture of shock and interpret these symptoms in the light of the foregoing concept.

The patient is pale, the lips are cyanotic, large beads of perspiration stand out on the forehead; he is oblivious to surroundings and lies motionless, with only occasional purposeless movements. If asked a question he will answer by "yes" or "no," but he will not volunteer any information. His respiration is shallow and, if shock continues, may become irregular; that is, of the Cheyne-Stokes type. Sometimes it is noisy (stertorous), or it has a sighing sound (sighing respiration). The temperature is subnormal—94 to 96° F. The patient is cold. The pulse is rapid and thready—140 to 150. The blood pressure is extremely low,

about 60 to 70 systolic. Sometimes there is an absence of diastolic pressure, but not often; if so, the prognosis is grave. The pupils are usually dilated.

There is a persistent low blood pressure due to a decreased circulating blood volume, although *rarely this may be due to a great and sudden* increase in blood volume. In either case there must be a prompt adjustment between the amount of blood and the vascular bed if tissues are to be properly nourished.

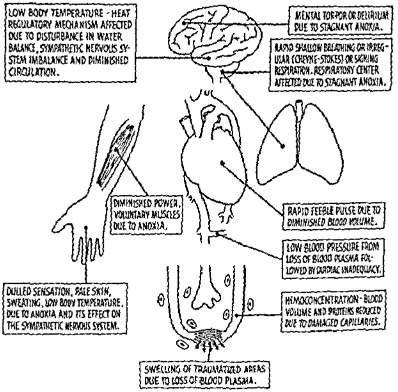

Fig. 107.—Diagram illustrating the clinical manifestations in shock and their probable causes.

Compensatory mechanisms come into play immediately. The carotid sinus reports a fall in pressure and there is vasoconstriction with cardio-acceleration—nature's way of raising blood pressure and increasing blood flow. The rapid thready pulse is evidence of an effort to race blood to the lungs which must breathe faster to provide sufficient oxygen. The stimulation of the respiratory center is due to anoxemia. As a result of peripheral vasoconstriction, the skin is pale and slightly cyanotic. This pallor varies in different kinds of shock. Thus in shock without blood loss pallor is accompanied by areas of cyanosis due to stagnation of blood in the venules; in hemorrhage which is severe there is very little cyanosis or there may be none because there is an insufficient amount of reduced hemoglobin; in infections the skin is plethoric. In any event the "peripheral tourniquet" is on to divert and hold blood in the vital centers. The skin is clammy and cold—evaporation through perspiration to

lower body temperature which in turn is necessary to slow the metabolism of cells so that they will not demand so much blood. So too, the lessened sensibility, mental dullness, and muscular relaxation are designed to conserve the need for blood; in short there exists a state of hibernation in which the body needs are reduced to a minimum so that vital centers may be kept alive with the diminished volume of blood.

The symptoms of shock reflect well-defined laws of physiology. We know that with vasoconstriction comes cardioacceleration, for this combination raises blood pressure. Conversely vasodilation and cardioinhibition is a combination which lowers blood pressure. Marey's law states that the pulse rate is inversely related to the arterial pressure and thus normally a rise in pressure causes a slowing of the heart rate. This is due to stimulation of the aortic plexus, afferent vagal nerves, or carotid sinus nerve. A fall in pressure is associated with an increase in heart rate.

The carotid sinus is a slight enlargement of the common carotid where it bifurcates into internal and external branches. Due to its rich nerve supply it is very sensitive to pressure changes. Chemical alterations in the blood affect the carotid body which may also produce changes in blood pressure and pulse rate so that mechanical or chemical alterations are detected and dealt with by these mechanisms. Compression of the carotid distal to the sinus, so as to raise the pressure in it, causes a slowing of the heart, vasodilatation, and a fall in blood pressure—this without the help of mechanically stimulating the vagus. Pressure proximal to the sinus, to produce a fall in pressure within the carotid, causes cardioacceleration, vasoconstriction, a rise in blood pressure, and liberation of adrenalin. The sinus has pressor and depressor effects. These are accomplished by the sinus reflex arc. The *afferent* component is by way of the sinus nerve a branch of the glossopharyngeal. Some fibers go to the carotid body (a sensory organ with functions like the sinus, sometimes the site of a tumor which must be excised). Centrally fibers make connections with the cardioinhibitory and vasomotor centers. The efferent fibers are composed of (a) a cardiac part by way of the vagus and (b) vasodilator and vasoconstrictors by way of the vagus and sympathetics.

A rise in the blood pressure of blood entering the right atrium causes an increase in heart rate—Bainbridge reflex. An inadequate amount of blood reaching the heart leads also to its increase in rate by way of the aortic and carotid sinus reflexes.

In shock normal physiological laws are operating but in various combinations. It is the summative effects of several factors—carotid sinus, aortic, visceral, somatic nerve stimuli; changes in blood volume, oxygen content, cardiac adequacy; and capillary permeability—all play a role in the excitation and integration of physiological processes which unite to conserve life and stop the vicious circle of shock.

Diagram of the Vicious Circle of Shock

$$\begin{tikzcd} & \text{Cardiac Inadequacy} \arrow[dl, shift left] \arrow[dr, shift left] & \\ \text{Anoxemia} \arrow[ur, shift left] \arrow[dr, shift left] & & \text{Diminished Circulating Blood Volume} \arrow[ul, shift left] \arrow[dl, shift left] \\ & \text{Vasoconstriction or Vasodilation} \arrow[ul, shift left] \arrow[ur, shift left] & \end{tikzcd}$$

A decrease in blood volume of less than 10 per cent produced by hemorrhage may elicit through constriction of central origin a decreased flow of blood through the submaxillary gland of more than 60 per cent even though accompanied by a rise in pressure. Indeed due to these mechanisms there may be an actual rise in blood pressure. Thus the diminished blood flow precedes the fall in blood pressure and this decrease in flow may be as much as 90 per cent before the pressure suddenly falls.

Anoxemia causes dilatation of capillaries with increased permeability and loss of plasma (Krogh). If oxygen is withdrawn for as long as three minutes, fluid escapes from capillaries at about four times the normal rate (Landis). Normal permeability can be restored within fifteen minutes by restoration of the normal blood supply which was diminished by the loss of plasma and water through the permeable capillaries.

This explains in part the difference between shock due to trauma in which increased capillary permeability is an initial derangement and shock due to hemorrhage in which capillaries begin to leak late due to anemic anoxemia. Shock will be delayed more in the latter, will be more amenable to treatment, and irreversibility will be postponed longer.

These are illustrations of the effects of injury on normal physiological processes and the great reserves present to protect and restore vital activities.

This clinico-pathologic picture of shock then is a synchronized dynamic mechanism invoked to sustain life—should it fail, irreversible shock ensues with peripheral vascular failure and blood is pooled in the skin. Although the causes are varied, the essential factor is a reduction in the circulating blood volume which results in disturbances of:

1. The central nervous system—caused by stagnant anoxia
   (a) Peripheral—dulled sensation
   (b) Central—mental torpor, or delirium
2. The sympathetic nervous system—caused probably by anoxia, sensory stimuli (in neurogenic shock), and reflex compensatory mechanisms
   (a) Pale skin, sweating, and low body temperature
3. The respiratory center—caused by stagnant anoxia
   (a) Rapid, shallow breathing
   (b) Irregular breathing (of the Cheyne-Stokes type); sighing or stertorous breathing
4. The circulatory system
   (a) Cardiac—caused by diminished blood volume
      (1) Rapid, feeble pulse

(b) Vasomotor—caused by primary factors (in neurogenic) or secondary factors (loss of blood volume), with arteriolar constriction and capillary dilatation
    (1) Low blood pressure
(c) Blood volume—due to damaged capillaries or loss of blood
    (1) Reduced (Mann found that normally 76 per cent of the total blood can be obtained from the large vessels of a dog at death. When death was due to shock, the large vessels yielded only 39 per cent of the total blood).

5. The heat regulatory mechanism—caused by disturbance in the water balance, sympathetic nervous system imbalance, and diminished circulation
    (a) Temperature usually low
6. The voluntary muscles—caused by stagnant anoxia
    (a) Diminished muscle power
7. The blood proteins—caused by loss of blood plasma through damaged *or dilated, and therefore more permeable, capillaries*
    (a) Low in amount

In general, we may speak of two forms of traumatic shock. The first is *primary* or *neurogenic* shock. This comes on immediately after injury and is presumably of reflex origin. It is characterized by an initial decrease in vasomotor tone with an early drop in blood pressure and a relative late decrease in cardiac output, the blood volume being unaffected. The second type is *secondary* or, as Burch and Harrison have called it, *hematogenic* shock. This comes on some time (an hour or two) after trauma and is characterized by: (1) a diminished blood volume, (2) an early fall in cardiac output, and (3) a relatively late fall in mean arterial pressure. *Collapse* has symptoms exactly like those of primary shock but is looked upon as having a functional rather than an organic cause and as being transitory in its action unless the disturbance is so severe that neurogenic shock results. However, Burch and Harrison use the term collapse synonymously with primary shock. It is perhaps common for primary and secondary shock to occur at the same time or follow each other. *Syncope* is synonymous with fainting. It is the mildest form of collapse.

HISTORICAL REVIEW

The term *shock* was first applied to this condition by James Latta in 1795. Travers in 1826 wrote on "An Inquiry Concerning Irritation" and called shock a "functional concussion." DeClasse in 1834, writing on "La Commotione," called shock an arrest of innervation. After Claude Bernard's discovery in 1852 of the sympathetic control of the blood vessels, Weir Mitchell, Moorehouse, and W. W. Keen in 1865 were the first to regard shock as a reflex motor paralysis. Loven in 1866 said that stimulation of the central end of a cerebrospinal nerve causes elevation instead of lowering of the blood pressure. Goltz's tapping experiments on frogs were written in a paper called "Klopfversuch" and caused Fisher in 1870 to reason that injury caused reflex paralysis of the vasomotor nerves, with a fall in blood pressure and a dilation of the great veins of the visceral region. Gross in 1872 poetically described shock as "a manifestation of a rude unhinging of the machinery of life."

Diagram of the Vicious Circle of Shock

Cardiac Inadequacy

Anoxemia

Diminished Circulating Blood Volume

Vasoconstriction or Vasodilation

A decrease in blood volume of less than 10 per cent produced by *hemorrhage may elicit through constriction of central origin a decreased* flow of blood through the submaxillary *gland of more than 60 per* cent even though accompanied by a rise in pressure. Indeed due to these mechanisms there may be an actual rise in blood pressure. Thus the diminished blood flow precedes the fall in blood pressure and this decrease in flow may be *as much as 90 per cent before the pressure suddenly falls.*

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This explains in part the difference between shock due to trauma in which increased capillary permeability is an initial derangement *and shock due to hemorrhage in which capillaries begin to leak* late due to anemic anoxemia. Shock will be delayed more in the latter, will be more amenable to treatment, and irreversibility will be postponed longer.

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4. The circulatory system
   (a) Cardiac—caused by diminished blood volume
      (1) Rapid, feeble pulse

The third step was to prove that if these various traumas were accompanied by a significant increase in the size and weight of the injured part, such increase was due to blood or blood plasma. After carefully studying the fluid from an injured part they found that, after mild trauma to an extremity, it contained a few red blood cells but was mostly plasma; after severe trauma to an extremity, the fluid consisted of whole blood; after burning an extremity, the fluid was clear and resembled pure plasma. After trauma to the intestines, the fluid contained some red blood cells but was mostly plasma. The fluid was in every case studied for chloride content, sugar content, and nonprotein nitrogen content and was found to be identical with normal blood plasma, although recent studies show a decrease in sodium and an increase in potassium.

The fourth step in the series of experiments consisted in studying the dogs with traumatized extremities at autopsy. Contrary to the opinions of previous observers, the great splanchnic areas and the intestinal tract were found to be pale and bloodless and the muscles in other parts of the body were found to have lost fluid. If a general toxin had been the cause of the shock, the reverse would have been the case.

Lastly, it seemed that the entire picture resembled one of hemorrhage, so the experimenters bled their animals of small amounts of blood at hourly intervals. They found that the results of taking whole blood are practically the same as those which follow trauma to an extremity. The results of taking pure plasma are practically the same as the results of burning an extremity.

Normally there is a free exchange of salts and substances of small molecular weight between the blood stream and the tissue spaces. This is not true of colloids, which are mainly proteins, because the blood vessels are normally impermeable to them. This is important, for the suction force (osmotic pressure) for the plasma normally counteracts the hydrostatic pressure of the capillaries. Since the fluid in the injured extremities has a protein content equal to that of the blood plasma, and since normally these proteins cannot go through the capillary wall, the proteins must have passed through the capillary wall because its permeability has been increased by capillary damage. Thus there results an osmotic pressure in the tissues equal to that of the blood, so there is no reabsorption of fluid from the injured extremity. The dehydration of the blood and the fall in the blood pressure does, to be sure, raise the effective osmotic pressure of the blood, and fluid is drawn in from healthy tissues all over the body, but this fluid is lost from the capillaries in the injured area. *Therefore, the loss of plasma proteins is the most important factor in the production of shock.* It is easy to understand, now, why shock due to trauma is more difficult to treat than is uncomplicated hemorrhage. In the latter we tie off the bleeder and restore the blood loss. After trauma, any procedure which increases hydrostatic pressure causes more loss of fluid through the injured, permeable capillaries. This is especially true after the injection of a crystalloid fluid, such as physiological salt solution. (Chapter 11.)

These experiments seem to clarify at least the cause of shock when induced by trauma to an extremity. However, it is well known that these explanations do not account for all forms of shock seen clinically. *There is one common denominator and that is a reduction in the circulating blood volume with loss of blood plasma.* In cases where the blood volume is reduced without a leakage of plasma from injured capillaries there is undoubtedly a loss of fluid to some extent, but this is so small that symptoms are transient. *Loss of plasma increases the hematocrit reading and accounts for the sustained symptoms and even death.* The mechanisms by which this reduction in circulating blood occurs are varied and each has been advanced as the cause of shock. The assembled evidence shows that any or all of these may be important in the cause of shock.

RECENT EXPERIMENTAL WORK

The Civil War and World War I provided an enormous stimulus for the study of shock. World War II with all of its modern scientific instruments of precision and perspicacious investigators also instigated the present quest for an answer to the prob

Crile thought that the circulatory failure was due to an exhaustion of the vasomotor center and the brain cells as a result of afferent impulses deluging the center. Mummery also believed this, but Porter, Mann, Ewing, and Janeway, Parsons and Phemister, and Blalock have shown that very prolonged stimulation of somatic nerves in mammals does not bring on circulatory failure.

Meltzer thought shock to be due to reflex inhibition, but Howell thought it due to stimulation of the cardioinhibitory centers.

Heidenhain in 1891 found that peptone, when injected intravenously into certain animals, produced marked exhaustion. Dale and Laidlow in 1910 described the paralyzing effect of histamine upon the capillaries. Dale and Richards in 1918 demonstrated so-called histamine shock.

It remained for the great physiologist, W. B. Cannon, to evolve the theory of the causation of shock that was accepted as the final word. Briefly stated, he contended that shock was produced by a metabolite (histamine) which injured the capillaries, causing them to dilate and remain paralyzed in that markedly dilated and therefore more permeable condition. During World War I he showed that if a soldier had a mutilated limb and a tourniquet was applied, shock did not follow, but if the tourniquet was released, shock ensued. He showed that traumatic shock was not a nervous reaction, for the spinal cord of animals could be divided and yet shock would follow. He thought he had proved, with the aid of Bayliss, that traumatic shock was not due to loss of blood in the part traumatized. It was his idea that shock may be the result of a dilation of the whole capillary system; that this capillary dilation is produced by a poisonous substance originating in the injured area and carried by the circulating blood; that the poisonous substance arises from proteolysis in the injured area; and that the circulatory failure in shock is due to a trapping of blood in the great capillary beds of the body, principally the splanchnic and muscular areas, and to the exudation of plasma through the permeable capillary walls. In other words, an individual bleeds to death in his own capillaries and that capillary blood may have an erythrocyte count which is 2 to 3 million higher than venous blood.

The work of Parsons and Phemister and of Blalock and his associates seems to rationalize the conflicting opinions of the causation of shock and to bring new light to this important subject.

First, the theory of a toxic substance causing shock seems to be partially disproved. Blood from an injured extremity, when absorbed by a dog or when injected into a normal dog, produces no symptoms. Blood from parts which have been traumatized by various means may be injected without producing any of the symptoms of shock. Traumatized muscle may be transplanted in various ways into normal animals without any symptoms of shock. The injection of histamine produces alterations in blood volume, plasma, red blood cell count, hemoglobin, and chloride content similar to those which occur after trauma, but the course of events is different. Hemorrhage and various types of trauma cause, first, a significant decrease in the output of the heart, and later, a drop in blood pressure. On the other hand, the injection of histamine causes first a decline in blood pressure and later a decrease in the cardiac output.

The second problem undertaken for solution was to determine whether or not there was a decrease in blood volume in shock, and if so, where this blood had gone. To solve this problem, dogs were anesthetized and their extremities were traumatized. In every case after sufficient trauma had been produced to bring about symptoms of shock, the traumatized extremities weighed approximately 3½ per cent of the body weight more than the normal extremities. Next, these experimenters decided to note the effect of burns upon the animal in the production of shock. They burned an extremity of an anesthetized dog and found that here, too, the burned leg weighed two and three-fourths per cent of the body weight more than the normal extremity. They next produced injuries to the intestines and here again found a marked increase in the size of the intestinal loops and mesentery and also a great increase in free peritoneal fluid.

Ischemic muscle necrosis, crushing injury, or crush syndrome was observed during World War II following air raids when people were pinned beneath falling debris from demolished buildings. Bywaters believes that plasma loss may play a role but renal failure due to the absorption of substances from the crushed muscle (myohemoglobin) is chiefly responsible. Others believe that extravasation of blood into body tissue, transfusion reaction due to incompatability, and crush syndrome are all related since they may produce hemoconcentration, hypotension, acidemia, and oliguria with acid urine containing creatinine. It is true that in crush syndrome there is myohemoglobinuria, whereas in the others there is usually hematuria and hemoglobinuria.

In this review many pertinent experiments have not been discussed. They may be found in the selected references at the conclusion of the chapter. It is the data more directly applicable to common clinical problems which has been summarized rather than the esoteric and turgid discussions of the pure researchers.

CLINICAL CAUSES OF SHOCK

Any sudden injury, local or general, functional or organic, mechanical, chemical, thermal or bacterial, accompanied by oligemia, hydremia, or plethora may lead to widespread dynamic adjustments to preserve that without which life is impossible—adequate blood and oxygen. To speak of the causes of shock therefore is to speak of all injuries to the body, because any kind of trauma, if sudden and severe enough, requires bold defensive changes to sustain life.

The injury which causes shock may have a single effect easy to interpret or it may have many consequences. For example, postoperative shock may be due to loss of blood, trauma to tissue, or prolonged anesthesia. It is easy to understand the first and second, but the third, anesthesia, may in turn produce shock through anoxemia, cardiac or respiratory failure, vasodilation, stagnant anoxemia due to prolonged immobilization, or shock from prolonged anesthesia alone. Infection may produce shock as a terminal event through toxic capillary stasis with loss of plasma and stagnant anoxemia, or through toxic myocarditis with cardiac incompetency, or through multiple septic emboli producing anoxemia plus vascular stasis; or, because of its extent, it may act as a burn with enormous loss of plasma through dilated and permeable capillaries; and lastly because of its suddenness and the amount of the antigen, the effect may include cerebral and cardiac damage with a swift and dramatic course as is seen in septic abortion, sudden flooding of the peritoneal cavity from a large perforation of a viscus—indeed this may simulate the injection of a syringe full of virulent streptococci directly into a large vein. In the list of clinical causes the effects will be mentioned briefly; then we shall discuss the effects in greater detail.

The clinical states which more commonly lead to shock may be listed as follows.

1 Loss of whole blood or plasma or both externally into body cavities or into tissues due to
   - (a) Loss of whole blood from severed heart or vessels due to
     - (1) Direct injury
     - (2) Operative blood loss
     - (3) Pathological changes in blood vessels such as ruptured aneurysm

lem. Although many questions remained unanswered, from it all has come some important observations which helped save lives during the World War II and which may be applied now in peacetime.

Moon and his colleagues speak of circulatory failure of capillary origin in which the gross and microscopic changes seen at post mortem show evidence of capillary damage such as dilatation, stasis, petechial hemorrhages, edema, and effusions present in extensive visceral areas, all due to capillary atony and tissue anoxia. They aver that the effects of hemorrhage and shock are entirely different, especially since in the former there is hemodilution and in the latter hemoconcentration. However, anoxia finally causes injury to capillary endothelium with leakage of plasma so that edema and hemoconcentration may be an end result. In this way shock begins with damage to capillary endothelium and hemorrhage ends that way. Wood and Blalock showed that hemoconcentration (erythrocytosis) per se does not cause shock. Fine, Frank, and Seligman believe that hemorrhagic shock is not apt to result in an irreversible state as rapidly as tourniquet shock. They found that transfusions may be curative even after the blood pressure remains at 30 mm. Hg. for hours, whereas transfusion is not curative if the blood pressure remains below 80 mm. Hg. for hours in tourniquet shock. They do not believe that the anoxemia in shock causes widespread capillary leakages. They used synthesized radioactive sulfur, bromine, and iodine in plasma proteins to prove their point. Plasma is lost especially in the injured area but irreversibility is due to decreased volume flow and velocity of the flow through the capillaries with a resulting cumulative adverse effect on vital organs or tissues, particularly the liver.

Richards introduced a long ureteral catheter into a median basilic vein, then along the axillary, then the subclavian, and into the right atrium. Forssmann had done this on himself more than ten years before. By this technique the pressure of blood in the right atrium and the total volume flow of blood or cardiac output may be measured. Shock was studied in this manner in human beings. The following observations were recorded: (1) there is an inadequate venous return of blood to the heart with diminished cardiac output; (2) a deficit in circulating blood volume is responsible.

Freeman believes that vasoconstriction may be an initiating factor in shock, whereas Wiggers criticizes this theory on the following counts: namely, that it has not been proved that the total resistance to the outflow of blood from the aorta is increased in early shock; that shock has not been produced by prolonged vasoconstriction due to stimulation of the sympathetics; that experimental and clinical hypertension in which total peripheral resistance is increased does not result in shock, and, finally, that adrenalin which is thought to cause shock in large doses actually produces deleterious effects on the coronary circulation and the heart. However, it is nevertheless possible to produce adrenalin shock without demonstrable coronary impairment.

Heymans demonstrated that the continuous secretion of epinephrine is reflexly controlled by afferent aortic and sinus nerves. Thus the carotid sinus is a nervous mechanism which controls the circulation directly through pressure changes and indirectly through chemical regulation. Weiss and his co-workers described three main types of cardiovascular response to carotid sinus stimulation: (a) *vagal*, characterized by marked asystole or sudden slowing of the heart rate, with or without marked fall in the arterial blood pressure; (b) *depressor*, characterized by fall in the arterial blood pressure without cardiac slowing; and (c) *cerebral* due to changes in cerebral circulation without slowing of heart rate and without a fall in arterial blood pressure. They found patients with spontaneous attacks of dizziness, weakness, and unconsciousness with or without convulsion. Pressure over the carotid sinus reproduced these symptoms. Denervation of the carotid sinus resulted in cure.

Barrow and Rhoads studied blast concussion injury abroad and experimentally here. Blast waves are irregular with many eddies in their periphery; they are reflected from surface to surface and are subject to augmentation or neutralization by other waves. It is the positive wave rather than the negative that causes most of the injuries to the lungs, heart, intestine, eyes, ears, and other organs. Negative wave may have some influence. In water there is only one wave and it is positive.

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(2) Operative blood loss

(3) Pathological changes in blood vessels such as ruptured aneurysm

(4) Heart rupture from coronary infarct
(5) Ruptured ectopic pregnancy
(6) Bleeding peptic ulcer
(7) Post-partum hemorrhage, etc.

(b) Burns, freezing—loss of plasma
(c) Trauma to body—loss of whole blood and plasma
(d) Trauma to intestines—loss of plasma chiefly
(e) Sudden removal of intra-abdominal pressure—loss of plasma and stagnation of blood in large veins (stagnant anoxemia)
(f) Fracture of long bones—loss of blood and plasma, rarely fat embolism
(g) Prolonged application of tourniquet—loss of plasma and stagnation of blood in large veins

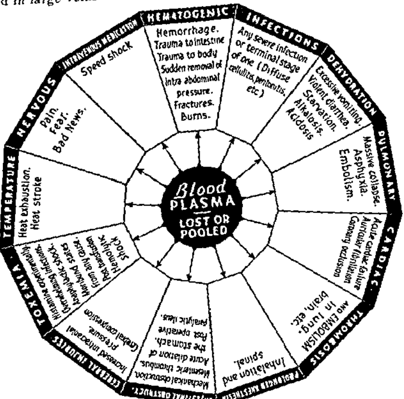

Fig. 108.—Diagram indicating some of the clinical causes of shock. In each instance blood plasma is lost through injured capillaries or pooled in dilated capillaries. In the latter instance, due to dilatation and stagnant anoxia, the capillaries become more permeable and here, too, plasma may be lost

(h) Crushing injuries, compression syndrome, extravasation of blood into tissues from any cause—loss of blood and plasma plus anuria and its effects
(i) Blast concussion—loss of blood and plasma
(j) Radiation sickness due to plasma loss into irradiated areas (Atomic bomb produced this in an acute fatal form)

2. Infection—Any severe extensive, or terminal stage of infection; sudden flooding with antigen caused by gas bacillus, streptococcus, staphylococcus in diffuse cellulitis, peritonitis, especially after perforation of a large ulcer or base of appendix or bullet wound—loss of plasma, stagnant anoxemia
3. Dehydration and starvation due to excessive vomiting, violent diarrhea, and accompanied by acidosis and alkalosis—stagnant anoxemia from hemoconcentration, anuria, toxic effect on capillaries also act as intensifying factors in other causes of shock such as hemorrhage and burns with local fluid loss and oligemia

4. Pulmonary mediastinal causes
   (a) Lungs
      (1) Embolism—due to sudden anoxemia, blockage of main arterial paths with resultant cardiac inadequacy, trapping of large amount of blood on the venous side due to decreased vis a tergo, and passive congestion
      (2) Massive collapse—chiefly anoxic anoxemia
      (3) Anoxemia from any cause—anoxic, anemic, stagnant, histiotoxic, or combinations
      (4) Paradoxical respiration
   (b) Pleura
      (1) Hemothorax—loss of blood and anoxia
      (2) Tension pneumothorax—anoxia venous stasis
   (c) Mediastinal shift or flutter—anoxia, venous stasis
5. Cardiac
   (a) Acute cardiac failure
   (b) Auricular fibrillation
   (c) Coronary occlusion
   (d) Cardiac tamponade

   Inability of heart to pump normal amount of blood because of weakness in heart itself, inability of heart to fill properly because of tamponade, inadequate amount of blood reaches heart, all of which results in decreased circulating blood volume due to pooling of blood on the venous side with stagnant anoxemia
6. *Thrombosis and embolism*
   (a) Mesenteric—loss of plasma and blood, bowel obstruction
   (b) Pulmonary—loss of plasma, anoxemia
   (c) Cerebral—cerebral compression with failure of respiratory, vasomotor, and cardiac centers
7. Anesthesia
   (a) Prolonged—probably due to stagnant anoxemia as well as anoxic anoxemia and reduction of circulating blood volume due to pooling; also cardiac and respiratory failure
   (b) Spinal—probably due to peripheral vasodilatation plus stagnation of blood in immobile extremities leading to reduced circulating blood volume and stagnant anoxemia
8. Acute intestinal obstruction
   (a) Postoperative
   (b) Paralytic ileus
   (c) Mechanical obstruction
   (d) Mesenteric thrombosis
   (e) Acute dilatation of stomach

Many factors involved in acute intestinal obstruction including dehydration with hemoconcentration and stagnant anoxemia, loss of plasma into peritoneal cavity, pooling of *blood into obstructed loops, anoxic anoxia due to interference* of descent of diaphragm due to distention, toxic factors.

9. Cerebral injuries
   (a) Increased intracranial pressure
   (b) Cerebral compression

Paralysis of vasomotor, cardiac, and respiratory centers due to pressure and ischemia; also loss of blood and plasma into brain tissue, skull, and scalp

10. Toxemia
   (a) Histamine, peptone, tissue extracts of muscle, adenylic acid, potassium injections experimentally—capillary poisons with loss of plasma and pooling in capillaries with anoxia

(4) Heart rupture from coronary infarct
(5) Ruptured ectopic pregnancy
(6) Bleeding peptic ulcer
(7) Post-partum hemorrhage, etc.

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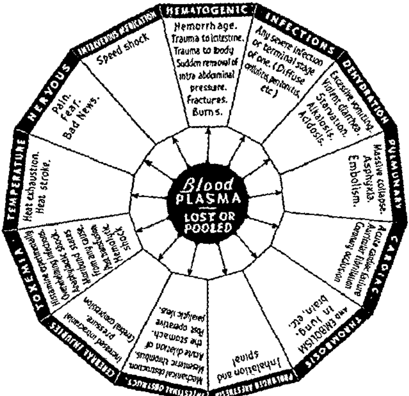

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total blood volume is unchanged, the circulating blood volume greatly reduced. The blood is pooled in the splanchnic vessels, which, because of their dilatation and the accompanying anoxia, become more permeable. In some types of shock the vasoconstrictors may be overactive.

Neurogenic shock due to fear, cold, or adrenalin may be explained by this response. Vasoconstriction produced by prolonged stimulation of the sympathetic nervous system in the normal animal leads to a decrease in the circulating blood volume. Following complete sympathectomy this does not occur. Vasoconstriction occurs in certain regions or

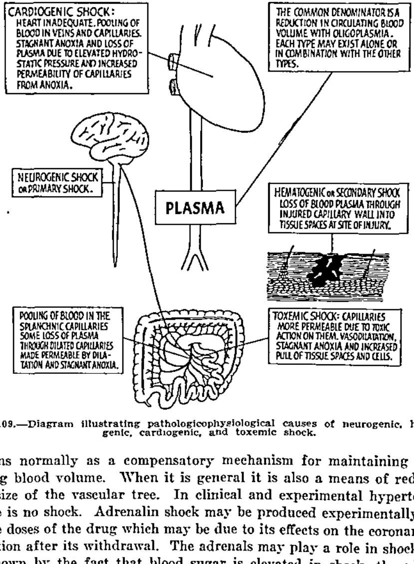

Fig. 109.—Diagram illustrating pathologicophysiological causes of neurogenic, hematogenic, cardiogenic, and toxemic shock.

organs normally as a compensatory mechanism for maintaining circulating blood volume. When it is general it is also a means of reducing the size of the vascular tree. In clinical and experimental hypertension there is no shock. Adrenalin shock may be produced experimentally with large doses of the drug which may be due to its effects on the coronary circulation after its withdrawal. The adrenals may play a role in shock; this is shown by the fact that blood sugar is elevated in shock; the adrenal cortex assists in regulating electrolyte balance, especially sodium and potassium, and influences the permeability of cells, including the capillaries; adrenalectomy causes death due to capillary atony, dilatation,

(b) Overwhelming infections
(c) Anaphylactic shock—bronchiolar constriction with anoxic anoxemia and capillary atony
(d) Hemolytic shock after blood *transfusions with incompatible blood*—*hemolysis*, capillary leakage, hemoconcentration, anuria
(e) Crush *syndrome*
(f) Drugs and poisons—may act on cell or capillaries

11. Moribund states from any cause—produce myocardial impairment due to primary (the heart itself), secondary (the result of infections or toxins), or tertiary (the result of hypotension) causes. Terminal shock is accompanied by vasodilation and capillary atony; there may be vasodilation, or vasoconstriction, the former leading to arteriolar and the latter to capillary stasis with a decrease in circulating blood volume with a reduction of the amount of blood returning to the heart and cardiac inadequacy
12. *Shift of blood into large veins*
    (a) In aviation—acceleration shifts blood into large veins (high positive) and the centrifugal effect *prevents blood from reaching right* auricle—also a drop in carotid and jugular pressure
    (b) *Sudden release of intra-abdominal pressure*
13. High or low environmental temperature
    (a) Heat exhaustion, "overheating"—heat retention, *since it cannot be lost* by radiation or evaporation if environmental temperature exceeds body temperature and is saturated with moisture—dehydration and loss *of sodium* chloride with vascular collapse
    (b) Heat stroke, "sun stroke"—heat retention due to loss of heat control, high fever, peripheral vasodilation with collapse
    (c) Freezing shock, cold exhaustion—fall in body temperature, depression of dissociation of oxyhemoglobin with anoxemia, peripheral vasoconstriction, capillary stasis decrease in circulating blood volume
14. Nervous
    (a) Severe pain—nociceptive stimuli may add to shock
    (b) Fear
    (c) "Bad news"
    (d) Overwhelming emotions of any type
    (e) Carotid sinus stimulation
15. Plethora, hydremic plethora, "speed shock"
    (a) Large quantities of blood given very rapidly when there has not been a *proportionate loss*
    (b) Rapid introduction of intravenous medication in great amounts
    (c) *Intravenous medication given* under pressure

Vascular system unable to expand quickly enough for the great increase in blood *volume; more blood in right heart* than can be pumped to the lungs with resultant cardiac incompetency; or multiple hemorrhages from rupture of small *vessels throughout the body and* blood extravasation syndrome with anuria

PATHOLOGICOPHYSIOLOGIC CAUSES OF SHOCK

Neurogenic or Primary Shock

Neurogenic or primary shock comes on immediately and is supposed to be due to an inhibition of vasoconstrictor fibers (and stimulation of undemonstrated *vasodilators) caused by prolonged activity* of the sympathetic nervous system. There is a decrease in vasomotor tone, with an early fall in blood pressure; then, later, a decreased cardiac *output*. The

reduced circulating blood volume. In this variety of shock, however, there is an actual loss of whole blood, plasma, or both, externally, into body cavities or into the tissues. As a result of this loss of blood volume there is cardiac insufficiency (low venous pressure in the vena cava causes the right atrium to be incompletely filled) and a consequent fall in arterial pressure. *In recovery from shock after blood or blood substitutes* have been given there is a rise in blood pressure before blood volume has been completely restored due to more adequate filling of right atrium. It is called secondary shock because it takes some time to manifest itself. This will vary with the amount of blood or plasma lost and the rapidity of its emergence from the circulation. However, when it does appear, the complete clinical picture is apparent instantly and dramatically. That is to say, a patient may leave the operating room in apparently excellent condition and all laboratory tests, including hematocrit, plasma protein, and blood counts may be normal, yet on arriving in his room he may suddenly go into a state of profound shock and may die unless measures are used promptly to restore the circulating blood volume.

If a frog's web is stroked gently, the capillaries will open; then new ones will be seen. After a time the web will get so thick that one cannot see through it. We learned in Chapter 3 that this is the exudative response to injury. This is due to a loss of plasma. If the stroking continues, capillaries will rupture and there will be loss of whole blood; the web will then be flooded with red blood cells. This experiment illustrates the cause of blood and plasma loss. If the area of the web is greatly exaggerated and if trauma of any kind is inflicted, then sufficient plasma will be lost to produce shock. Tourniquet shock results after a tourniquet is released from an extremity. The surface of a leg represents roughly 18 per cent of the body surface; the interior of the leg filled with muscles which contain over 700 capillaries per cubic millimeter is a veritable lake of vascular space. When a tourniquet is applied, no blood enters or leaves the extremity. *Capillaries are dilated* due to paralysis of vasoconstrictors and the accumulation of metabolites (H substances) in the tissues. Capillaries are more permeable because they are dilated and because the endothelial cells are damaged by anoxia. When the tourniquet is released, shock ensues; it will be more profound the longer the tourniquet is on prior to its release because capillaries will be damaged more If the tourniquet is released at intervals, if the leg is packed in ice if firm pressure is applied to the extremity by elastic bandage, shock will be less severe when the tourniquet is removed because less plasma will be lost.

Fine and his co-workers tagged plasma with radioactive substance and found that plasma is lost in shock at the site of injury but not all over. As shock deepens, about one-fifth of capillary blood becomes stagnant. The progressive decline in shock is due *principally to a fall of*

stasis, and peripheral vascular stagnation. *If there is sudden and prolonged vasoconstriction, shock occurs. This type may also be seen as a result of stimulation of vasomotor center by chemical or mechanical agents such as local anesthesia and operation in upright position.* If the vasoconstriction is slow in evolving as in hypertension, shock does not occur. This is true in hemorrhage, brain tumor, or any other factor which may destroy life. When compensatory mechanisms have a chance to adapt the organ or organism to its handicaps, symptoms may be few and obscure. When the are found to act suddenly, symptoms are severe and prominent. It is well to remember that vasodilation as seen in spinal anesthesia leads to arteriolar stasis and will be benefited by adrenalin. Vasoconstriction leads to capillary stasis and will not be helped by the drug. This is seen in hematogenic shock where vasoconstriction is an attempt to compensate for the reduced blood volume. The arterioles are constricted and the capillaries are dilated and lose blood plasma. Capillary pressure rises due to an increase in the proportion of blood cells and the resulting viscosity, which slows the circulation and permits a greater transudation of fluid from the vessels. A vicious circle is thereby induced until the blood pressure falls to a critical level; then vasodilatation occurs and death may follow. Neurogenic shock is transient as a rule. Fear, anger, "bad news," or pain may cause it.

W. B. Cannon *found that soldiers who were hungry or cold would go into shock with a small wound but that soldiers who were warm and well-fed could stand much pain. If the blood pressure is low, the heart will not have sufficient blood to pump and stasis will occur in the capillary beds, and ultimately secondary shock may result due to increased permeability of the capillaries from stagnant anoxia. In spinal anesthesia the constrictor response to hemorrhage is abolished and therefore hemorrhage and shock are apt to occur.*

Neurogenic shock is apt to be due to *carotid sinus stimulation. Depressor type syncope* is seen in predisposed *persons with a tendency to* postural hypotension *after prolonged bed rest, debilitating conditions such as fatigue, fasting, severe anemia, or other disease, standing at attention for long periods, or standing in crowds. Syncope due to standing in crowds or standing at attention may be due to pooling of blood in the veins of the legs and abdomen. The heart rate is not slowed;* the blood *pressure is low. Vagal type. Syncope may occur* with slowing of the heart *or asystole and consequent fall in blood pressure. Cerebral type. This manifests itself without slowing of heart or fall in blood pressure but with convulsions and hyperpnea.* This type is probably due to a disturbance of the blood supply to the carotid body.

Hematogenic or Secondary Shock

Hematogenic or secondary shock occurs, as the name implies, from loss of blood plasma. This is a misnomer because all shock is due to a

reduced circulating blood volume. In this variety of shock, however, there is an actual loss of whole blood, plasma, or both, externally, into body cavities or into the tissues. As a result of this loss of blood volume there is cardiac insufficiency (low venous pressure in the vena cava causes the right atrium to be incompletely filled) and a consequent fall in arterial pressure. In recovery from shock after blood or blood substitutes have been given there is a rise in blood pressure before blood volume has been completely restored due to more adequate filling of right atrium. It is called secondary shock because it takes some time to manifest itself. This will vary with the amount of blood or plasma lost and the rapidity of its emergence from the circulation. However, when it does appear, the complete clinical picture is apparent instantly and dramatically. That is to say, a patient may leave the operating room in apparently excellent condition and all laboratory tests, including hematocrit, plasma protein, and blood counts may be normal, yet on arriving in his room he may suddenly go into a state of profound shock and may die unless measures are used promptly to restore the circulating blood volume.

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Fine and his co-workers tagged plasma with radioactive substance and found that plasma is lost in shock at the site of injury but not all over. As shock deepens, about one-fifth of capillary blood becomes stagnant. The progressive decline in shock is due principally to a fall of

actively circulating plasma rather than to a continued loss of this vital fluid. After it has been replaced, velocity flow must be restored before vital tissue processes are lost. The truth of this statement is confirmed at autopsy in patients dying of shock. Often enormous quantities of plasma and blood are introduced, even under high positive pressure. The volume is thereby completely replaced, but if the heart does not circulate it, the body cavities will be full of plasma and actually hasten death. Anoxemia, from any cause, will increase capillary permeability in shock; this is stagnant or anemic anoxia—all capillaries begin to leak under such conditions.

Secondary shock is due to a loss of blood plasma into the tissues. Hematocrit readings and plasma protein studies show this to be true because there is a great decrease in plasma and an increase in cells. This is perhaps the only way in which shock due to hemorrhage can be differentiated from shock due to loss of blood plasma. However, if bleeding is long continued, enough plasma will be lost to reduce osmotic pressure in the capillaries. They will also become more permeable due to anoxia (caused by the constricted arterioles and reduced volume flow as well as the hemodilution). Capillaries become permeable and fluid is lost in the tissues with resulting edema (Chapter 11). Finally in hemorrhage there may be hemoconcentration. Thus traumatic shock begins with capillary injury, whereas hemorrhagic shock ends this way.

Erythremia in shock may be due in part to splenic contraction. Page and Glasser found that 50 per cent of the increase in red blood cells results from this cause in intestinal manipulation shock and 65 per cent in tourniquet shock. Perhaps the increase in adrenalin during shock may be partly responsible for splenic contraction.

Blood viscosity is increased due to loss of fluid into the injured tissues; this increases the tendency for pooling in the hyporeactive capillaries reducing the circulating blood volume.

By referring to the chapter on hemorrhage we see that the clinical symptoms of shock due to loss of whole blood and shock due to loss of plasma are the same. However, in hemorrhage, when bleeding is controlled symptoms abate and transfusion is curative even after the blood pressure has been as low as 30 mm. Hg for hours. This is not true of traumatic shock in which the capillaries continue to lose plasma twenty-four to forty-eight hours after the injury. Even in severe trauma, where capillaries are actually ruptured, the loss of red blood cells soon ceases due to clotting, but plasma continues to be lost.

Cardiogenic Shock

In cardiogenic shock there is first a cardiac inadequacy and then a fall in arterial blood pressure due to a pooling of the blood. The patient is cyanotic and the veins are distended (especially in the neck). Clinically this type is seen in auricular fibrillation, coronary occlusion, and

acute cardiac failure and in cardiac thrombosis and embolism. There is no actual loss of blood, yet the quantity of circulating blood is suddenly reduced. Venous pressure is greatly increased, venules and capillaries are greatly dilated, arterioles are constricted. Soon leakage of plasma occurs, for dilatation and increased permeability of capillaries go hand in hand and stagnant anoxia enhances the process. In addition, the dyspnea which accompanies cardiac failure increases the negative pressure in the thorax (see Chapter 19). Thus there is an increase in pulmonary venous pressure and also an increase in the negative pressure within the thorax. This results in pulmonary edema and increased anoxia.

Toxemic Shock

Toxemic shock (vasogenic) is due to a toxin in the blood. This form of shock may be produced in animals experimentally by injecting histamine. Most observers believe that the death of the injured soldier which Cannon describes as having occurred after the release of a tourniquet on a mangled extremity was caused by a sudden rush of blood into the damaged capillaries, with a great loss of blood plasma. Tourniquets placed on extremities in experimental animals for any length of time will produce shock when released. This, according to Allen, cannot be entirely explained on the theory of loss of blood plasma. The capillaries are more permeable (due to paralysis of vasoconstrictors, local asphyxia, and capillary damage caused by stasis), but the tissue spaces and cells are rendered more able to accept more plasma by the toxic factor. After injection of histamine the blood becomes more concentrated as a result of a loss of "free" water and the muscles gain water (Robinson and Parsons). Thus the old idea of a patient "bleeding to death in his own capillaries" is only partially correct, for in addition he loses plasma and water into the tissues. *Far from being obsolete, this theory undoubtedly explains the permeability of capillaries in infections with great edema and loss of plasma into the affected area—from the simple localized swelling of a boil to the widespread loss of plasma in peritonitis.* Perhaps also in extensive burns this theory may explain in part the cause of local and general capillary permeability. It is perhaps a causative factor in infection, dehydration, moribund states from any cause, and posttransfusion shock.

Many of the chemicals used to produce toxemic shock experimentally have been mentioned under Clinical Causes of Shock. There is reason to believe that toxins play a role because of recent experimental and clinical observations. Some of these should be reviewed. After crushing injuries or burns a sludge forms in the injured vessels; this may be initiated by local tissue toxins and may contribute to a toxemia by multiple emboli or the release of toxic substances from the "sludge." Potassium is increased in shocked animals probably due to damage of tissue cells. However, its toxicity increases six to nine times. This is not true of

actively circulating plasma rather than to a continued loss of this vital fluid. After it has been replaced, velocity flow must be restored before vital tissue processes are lost. The truth of this statement is confirmed at autopsy in patients dying of shock. Often enormous quantities of plasma and blood are introduced, even under high positive pressure. The volume is thereby completely replaced, but if the heart does not circulate it, the body cavities will be full of plasma and actually hasten death. Anoxemia, from any cause, will increase capillary permeability in shock; this is stagnant or anemic anoxia—all capillaries begin to leak under such conditions.

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resemble traumatic shock, if he is to prevent and treat the syndrome correctly. The chief causes of this type of shock are (1) paradoxic respiratory movement of the thoracic wall with resulting cardiorespiratory incompetence and anoxemia; (2) anoxemia from the accumulation of blood or secretions in the tracheobronchial tree; (3) atelectasis from (2); (4) atelectasis from exhaustion due to labored breathing and frequent ineffective coughing; (5) undue pressure on the lung and mediastinum by (a) the accumulation of large amounts of serum in a wound after rib resections, (b) collapse of the thoracic wall over an intrapleural air or fluid space in which the pressure has not been reduced by aspiration before operation, (c) too great thoracoplastic collapse of the thoracic wall at any one operative stage, (d) too large an intrathoracic packing, (e) too tight a dressing after resection of ribs, (f) abdominal distention; (6) too negative a pressure in the pleural cavity in which the lung cannot expand freely because of stiffness of the visceral pleura.

Crush Syndrome, Ischemic Muscle Necrosis, Traumatic Edema, Traumatic Anuria.—Crush or compression syndrome, ischemic muscle necrosis, traumatic edema, traumatic anuria are terms applied to an injury which results in shock due to burial beneath debris in air raid casualties. This has been discussed in the Historical Review in this chapter. The causes have been listed as toxins, loss of plasma, or autolytic products from dead or dying muscle, injured kidney tubule cells, and precipitation of myohemoglobin in the tubules due in part to renal vasoconstriction with oliguria which favors the intrarenal precipitation of myohemoglobin. The one big factor seems to be a wide area of muscle necrosis due to ischemia, direct compression, or interference with blood supply of the muscles. Early there is a local loss of plasma and fluid; later there is the absorption of a toxic product which produces anuria and uremia. The small quantity of urine which may be excreted contains (if kidney has been torn) some blood pigment which resembles hemoglobin but is, in fact, myohemoglobin, casts, high chloride, high potassium, and creatinine. The blood shows hemoconcentration, high potassium levels, up to twice the normal, and azotemia. Oliguria due to mismatched blood transfusion, oligemic hypotension, wide extravasation of blood into body tissues, and crystal calculi must be differentiated. Hematuria and hemoglobin may be differentiated by examination of the urine—the history is all important.

Blast Concussion.—Injuries may occur due to air or water waves producing shock (see Historical Review). These waves are irregular in outline near the source with eddies in the periphery. Blast waves, like sound waves, are reflected from surface to surface and are subject to reinforcement or neutralization on meeting a similar wave in the same or opposite phase. Pressures vary as the square or cube of the distance from the source. Although there is a negative wave after a blast, this is said to have less influence than the positive wave. In water there is only the positive waves, although if shallow a rebound wave would occur which

magnesium and other substances. The injured area loses potassium and takes on sodium. Thus the blood is low in sodium and higher in potassium. Enough sodium is lost in a traumatized extremity to equal the total amount in the circulating blood and one-fourth that of the total extracellular fluid. Potassium is excreted in the urine in shock. Sodium is not, even after giving it. This means dehydration of the intracellular compartment. Since the blood constitutes only about one-fourth of the sodium reservoir and since the loss is more than the total amount contained in plasma, much sodium must be lost in the tissues (see Chapter 6, Burns, and Chapter 11). Radiation sickness, like high intestinal obstruction, may cause shocklike symptoms due to toxemia or H substances. The protracted symptoms and perhaps the irreversible types of shock may be due to the systemic absorption of toxic substances bacterial in origin produced in crushed muscle, although there is no proof of this recently revived old theory.

In summarizing the present-day knowledge of shock, we must assume that no single factor is responsible. Many of the causes which have been discussed may act at the same time and no doubt all may play an important role in a single case. A common occurrence is to see primary shock from pain followed by secondary shock from blood loss, the patient remaining in shock continuously.

Special Types of Shock

Thoracic.—Following World War I and the advent of major chest surgery, we have learned that in addition to the other causes for shock already mentioned tension pneumothorax presents a special problem. This will be discussed again in Chapter 19. An open wound in the chest (sucking wound) may build up air pressure and in addition fluid pressure if there is bleeding within the thorax and produce profound shock and death due to (1) collapse of the lung on the injured side; (2) reduction of respiratory capacity of the opposite lung from the paradox in respiration transmitted from the injured side (mediastinal flutter), or if there is no flutter there will be a mediastinal shift interfering with respiration of the sound side; (3) reduction of circulatory efficiency by interference with venous return (especially on the right side); also by twisting and shifting the heart induced by the rotary motion of the heart beat; this will also have an effect on the extracardiac autonomics which may not only affect the beat, but the vasomotor mechanism as well (central and peripheral) through aortic and carotid sinus mechanisms. Cardiac tamponade produces shock rapidly. Here a wound of the heart permits the accumulation of blood in the pericardial cavity, restricting cardiac movement.

Obviously surgical shock may occur from thoracic operations from causes already discussed. There is, however, a special type of shock which the thoracic surgeon must recognize, even though the symptoms and signs

the process unless there is, in addition, sunburn. In sunstroke the skin is hot and dry and body temperature may reach 108 to 110° F. The prognosis is grave.

Freezing shock occurs from six to twelve hours after thawing in experimental animals. Extracellular water is decreased, plasma sodium is increased, water enters body cells. In addition, shock may occur from associated factors such as arteriolar relaxation with capillary atony as in tourniquet shock; also thrombosis and embolism (see Chapter 4).

Cold exhaustion. Fatigue and cold produce a desire to sleep. When the body lies motionless in low environmental temperatures, body heat is lost and body temperature falls. At 68° F. coma sets in and death occurs. The fall in temperature depresses the dissociation of oxyhemoglobin and tends to lower oxidation in the tissues (Wright).

COLLATERAL CHANGES IN SHOCK

As a result of deficient blood flow and oxygen supply most organs are temporarily impaired. The *liver* suffers greatly. In shock there is an increased breakdown of protein in the peripheral tissues; this affects chiefly the muscles. There is also a delay in the regeneration of serum protein. Hepatic glycogen decreases and its synthesis from administered glucose is delayed. Metabolic transformation of amino acids is slowed and there is a rise of amino acids in the blood in shocked animals; the rate of urea formation from amino acids is depressed. The loss of potassium from cells may be a toxic factor in shock. Water and potassium are lost from liver cells to extracellular spaces. During recovery there is a tendency for replacement of lost potassium but not complete. Thus we have liver impairment as a result of shock which may tend to perpetuate or at least act as an augmenter of the syndrome. This explains, at least in part, the hypoglycemia, the increase in amino acids, the acidosis, the decrease in serum protein even after capillaries cease their leakage in shock.

The kidneys also are impaired, as indeed are all the cells, from the decrease in blood and oxygen which reaches them. Their particular deficiencies are not entirely known but enough is understood to govern our therapy. The body as a whole and each of its cells are functioning on a minimum supply of food and oxygen. The sooner these requirements are met, the less will be their impairment. Therapy is directed to replace blood, plasma, water, electrolytes, and glucose. It is unreasonable to suppose that the liver can synthesize amino acids into serum proteins during shock or that the kidneys can take out all water and electrolytes not needed. These facts lead the surgeon to selective and judicious treatment in kind and amount. Shock unabated or improperly treated may lead to irreversible changes in cells.

would coincide with the former. As a result of this injury, traumatic lesions are found in the lungs with hemorrhages adjacent to the bronchi, lacerations of the lungs along the line of the ribs, and red hepatization associated with cyanosis, dyspnea, cough, and hemoptysis. Hemorrhages in the intestines and other abdominal organs with pain, distention, absence of peristaltic sounds, and all the symptoms and signs of paralytic ileus may follow immersion blast. Perforation of the intestine is not uncommon and there may even be evisceration. The eyes and ears may also be injured by blast. Shock is profound but usually is accompanied by bradycardia, at least during the early period following injury.

Acceleration Shock.—Acceleration shock is the name given to shock caused by a sudden and extreme change in speed. "G" is the gravitational force on a freely falling body. In aviation acceleration which causes blood to leave the brain is said to be positive and that which causes a sudden rush of blood to the brain, negative. High positive (black out) or negative (redding out) may produce shock. The former is more common and is seen as the plane comes out of a dive. Blood leaves the brain and thorax to enter the large abdominal veins. Since there are no valves in the vena cava and its principal branches (except azygos and spermatic), this is easily accomplished under the terrific force. There follows a drop in carotid and jugular pressures. The centrifugal effect prevents blood from reaching the right atrium. This results in cardiac inadequacy and a fall in blood pressure.

At 5 "G's" the body is beyond control of the muscles except for slight movements of the arms and head. At 7 "G's" there is a failure of filling of the heart. At 20 "G's," which is an acceleration of 640 feet per second, concussion occurs in a fraction of a second. Since the jugular veins have valves, a sudden rush of blood to the brain as the plane descends at a bulletlike speed is unlikely; should it occur the symptoms would include a transitory unconsciousness as in concussion; some attribute this to fat emboli in the finer cerebral blood vessels.

Shock Due to Extremes in Environmental Temperatures.—Shock due to heat has been discussed under "Clinical Causes of Shock. *Overheating* or *heat exhaustion* is due to environmental temperatures above body temperature so that body heat cannot be lost by radiation. If, in addition, there is much moisture in the air, body heat cannot be lost by evaporation. The cerebral heat-regulating mechanism is normal but the body cannot keep its normal temperature because the methods used by the body to lose heat are not effective. The victim goes into peripheral vascular collapse or syncope probably from neurogenic or carotid sinus effects. The oral temperature may be subnormal and the skin is cold and clammy. The prognosis is good.

Sunstroke is due to heat retention caused by a disturbance of the heat regulation centers. The actinic rays of the sun are not involved in

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thirty minutes because its course offers one of the best guides to prognosis and treatment. Yet it has been noted that about 5 per cent of severely injured will show a transient rise in blood pressure for several hours even though other clinical signs are typical for shock. Such patients must be watched closely for they suddenly have a precipitous fall in blood pressure. The reverse is also true in that patients with minor injuries may have a very low blood pressure probably due to vasovagal collapse. A third group in shock may maintain a normal pressure as long as they are recumbent—should they sit or stand the blood pressure falls rapidly.

The pulse is unreliable in the diagnosis of shock although it is usually fast. In vasovagal syncope it is slow and sometimes it may be slow in severe hemorrhagic shock. More often it is fast due to fear or excitement out of all proportion to the loss of blood volume. As a rule, however, the pulse varies inversely with the blood pressure and is useful in prognosis and diagnosis in relation to the pressure.

The skin is very unreliable in the diagnosis of shock yet as a rule it is pale, cold, and clammy. A few simple experiments will illustrate the variations in skin color. If a blood pressure cuff is placed on the arm of a normal individual, held at the level of the heart, and is inflated above systolic pressure the arm becomes pale and ashen, and the nail beds become cyanotic. This resembles shock without blood loss. Arterial color replaces the cyanosis on release of the cuff, indicating a good circulation. If now the same test is repeated with the arm held high above the head before the cuff is applied, there will be extreme pallor with only a little cyanosis in the nail bed. This resembles the color of the skin in hemorrhagic shock and shows the greatest diminution of blood in the skin. Lastly, if the same experiment is tried with the arm hanging down, there is a bright red-purple color and finally deep cyanosis—the counter part of shock from massive infection.

The clinical symptoms and signs of shock are generally as depicted; however, variations do occur and it is the combination of symptoms and signs which leads to accurate diagnosis.

Laboratory Aids in Diagnosis of Shock.—Hemoconcentration is probably the most frequently used single factor for the recognition of shock.

A hematocrit reading reveals a low plasma-high cell ratio. The red blood cell count will be high. A rise from 5 to 6 million cells represents a concentration of 20 per cent. This, according to Moon, indicates that the total blood volume has been reduced about 10 per cent and the plasma volume, 20 per cent. Hemoconcentration of 40 per cent (count of 7 million) is always accompanied by all of the clinical symptoms and signs of shock. The specific gravity of the blood roughly parallels the hematocrit readings: that is, it will be increased in hemoconcentration. Hemoglobin readings will rise with the increase in cells.

IRREVERSIBLE SHOCK

The term irreversible shock is used to denote the syndrome with peripheral vascular failure which does not respond to remedial measures. Since in most instances the principal cause is a decrease in circulating blood volume, in the irreversible phase life cannot be sustained even if the blood volume is restored completely.

Clinically irreversible shock is seen in severe infections, lesions involving the central nervous system, anoxic anoxemia due to pulmonary damage, and a long-persisting combination of anemia, oligemia, and hypotension with terminal signs of myocardial insufficiency.

We have noted that hypotension due to hemorrhage is better borne than that due to extensive capillary damage, although ultimately in either event, stagnant or anemic anoxia causes all capillaries to leak, and plasma or fluid introduced under pressure will be lost in the pleural, peritoneal, pericardial, and meningeal spaces later in the subcutaneous tissues. There is also a failure of cellular metabolism in irreversible shock. In fact, many organs, especially the brain and heart, resist anoxia less than the capillaries. This is borne out by the fact that there is a depression of respiration and damage to heart cells before capillaries begin to leak especially in shock due to generalized infection; this is due to the destruction of cells by interference with the enzyme systems. *Irreversible shock then is due to the permanent damage of heart cells, brain cells, and capillary endothelium from prolonged circulatory failure.*

DIAGNOSIS OF SHOCK

Shock is easily diagnosed by the symptoms and signs previously enumerated. The particular type of shock may be ascertained by a brief history of the injury or disease and by laboratory aids. No single symptom or sign or laboratory finding is diagnostic. Even the knowledge of the exact amount of blood lost will not permit the prediction of shock. The average adult will tolerate the acute loss of one liter of blood without shock except the vasovagal type of collapse. Profound shock with systolic blood pressure of 60 mm. Hg or less usually means a loss of 2 liters of blood. Yet profound shock may occur from the loss of less than 1 liter.

People who are injured may have pre-existing conditions which enter into the picture such as dehydration, microcytic anemia, cardiac failure, etc. Moreover, there is no way of predicting how far the compensatory mechanisms will go in preventing shock. Lastly, irreversible shock may often be anticipated but should not be invoked as a deterrent for active treatment.

Let us consider (a) the usual clinical symptoms and signs, (b) variations, (c) laboratory data, and (d) modifications.

The most reliable clinical means of diagnosing shock is a persistent fall in arterial pressure. In suspected shock this should be taken every

(7) Differences in capillary and venous plasma protein and hematocrit values—blood proteins sometimes show a slight difference in values taken from capillary and venous blood—the former may be slightly higher because it is diluted less with intercellular tissue fluid. Thus there may be a higher protein and a higher hematocrit in capillary blood than in venous blood, the higher protein due to loss of water first and plasma later, the higher hematocrit due to loss of water earlier with less dilution than in veins. Other blood changes include a decrease in platelets in *shock and an increase in potassium and a decrease in sodium.*

Laboratory aids are very useful in the diagnosis and treatment of shock. With the copper sulfate method the hematocrit and plasma protein values may be obtained quickly and accurately. Blood counts and hemoglobin determination are also easy to obtain and aid in evaluating the necessity for plasma, whole blood, or water. The quantity and specific gravity of the urine is an indication not only of the water balance (q.v.) but also of the osmotic index of the blood. However, finally one must consider all laboratory tests in the light of clinical symptoms and signs which, after all, constitute the only real method of diagnosis.

Surgical Shock

A surgical operation is an experiment in which the knowledge and skill of the physician is pitted against the ravages of disease. It is the surgeon's duty to evaluate the patient's ability to stand surgery and to *prepare* him for the ordeal. He must be meticulous in the conduct of his operation and then meet the requirements necessary to assure recovery after the operation has been completed.

Preparation for Surgery (Preoperative Care).—In the list of aphorisms (Chapter 1) we have seen that, "There is no operation that has merit enough to be used on a patient who cannot stand it." To put the patient in good condition we must determine how he varies from the normal due to (a) the disease, (b) his deficiencies caused by the disease, and (c) complications. Thus if the patient is normal he needs no preparation except to combat fear and to secure rest before the operation by the use of sedatives. If he is deficient, much treatment may be necessary before surgery can be safely done. Although every need of the patient cannot be discussed here, it is important to emphasize that attention to details may prevent a chain of events leading to shock. What normal requirements must be fully met if the shock is to be prevented?

1. *Oxygen-Anoxemia.*—Anoxemia from any cause must be combated (anoxic, anemic, stagnant, histotoxic, or combinations). Eliminate cause if possible and give oxygen.

2. *Blood.*—Quantitative or qualitative deficiencies may be due to disease of blood-forming organs, excessive loss of blood, or a disproportion between the volume of circulating blood and the vascular bed. Give

Hemorrhage may be differentiated from shock by these studies, for the blood will be diluted within two hours or more after bleeding occurs. Blood counts and hemoglobin will be low. In shock due to hemorrhage hemoconcentration may be present, but to a lesser degree and very late. However, if hemorrhage is due to capillary trauma (extensive injuries by blunt force) hemoconcentration gradually develops and equals that seen in burns, trauma to the intestines, intestinal obstruction, or other types of shock.

Based upon this observation, Phillips, Van Slyke, and associates have described the copper sulfate method for measuring specific gravities of *whole blood and splasma. Their line charts for calculating plasma proteins, hemoglobin, and hematocrit from plasma and whole blood gravities offer a quick method of obtaining accurate information in a* very few minutes.

Since hemoconcentration is not a regular feature of shock except in burns and crushing injuries, it *must be interpreted as one of* the symptoms in diagnosis and as a guide to treatment. Indeed experiments show that hemoconcentration per se does not cause shock—it is the reduced blood volume and anoxia.

Plasma proteins are low when plasma has been lost, high in hemoconcentration due to water loss, and low after hemodilution in hemorrhage. Blood volume is reduced and the extent of this reduction may be ascertained by the use of Evan's blue dye as described in Chapter 13, albeit this is still an unhandy procedure.

Hematocrit, plasma proteins, and chlorides may be normal yet total volume so low that life cannot be sustained. Many factors may contribute to this incongruity: (1) *Lack of hemodilution—after hemorrhage and before the fluid shift from intercellular tissue spaces has occurred,* the various constituents, though *reduced* in total quantity, appear to be relatively normal because there has been no hemodilution; studies of the total volume by Evans blue T-1842, as described in Chapter 13, will disclose the amount of blood lost. (2) Pre-existing microcytic anemia—in microcytic anemia a normal hematocrit may mean hemoconcentration. (3) Pre-existing polycythemia vera—in polycythemia vera, on the other hand, a *high* hematocrit may mean a normal ratio for that individual. (4) *Increased volume of the red cells after hemorrhage—one to two days* after hemorrhage *due to the low osmotic pressure* red blood cells may swell and take more volume than they should. (5) Dehydration—in dehydration even though plasma and cells have been lost, hematocrit may be normal. (6) Differences in capillary and venous blood counts—in wound shock red blood counts from the finger tip (capillary blood) may be 2 to 3 *million* higher than from venous blood. Presumably a similar difference of *30 to* 40 per cent occurs in the *hemoglobin. This is probably due to the fact* that the *peripheral "tourniquet" has been put on*—arteriolar constriction with *capillary* stasis and therefore increased hemoconcentration.

6. *Environment.*—The patient should be kept at about room temperature—70° F.—warm not hot.

7. *Asepsis.*—Strict asepsis should be observed.

8. *Blockage of Afferent Nerve Impulses.*—There is no proof that blockage of afferent nerve impulses through the use of local or spinal anesthesia prevents shock.

After the Operation.—How has the surgical procedure interfered with the normal body requirements? If not at all, relieve pain which may cause shock and nothing more. Excessive and unnecessary treatment is a burden on the patient and may have serious consequences (see Chapter 13).

Common interferences are:

1. *Oxygen Consumption.*—After open chest operations there may be anoxic anoxemia. However, all types of anoxemia may occur and demand correction. The following measures may be helpful: oxygen inhalation, aspiration of the trachea and bronchi by catheter suction or bronchoscopy, deep breathing, adequate negative pressure on the operated side (see Chapter 19), and blood transfusions as needed.

2. *Loss of Blood and Fluid.*—Loss of blood and fluid inadequately replaced during surgery or being lost afterward due to drainage or postoperative hemorrhage demands transfusion and infusions of water and electrolytes—avoid dehydration.

3. *Inability to Take Fluid or Food or Assimilate It.*—This must be provided by the use of plasma, protein hydrolysates, glucose, and sodium chloride and vitamins.

4. *Elimination.*—Elimination must be maintained by catheter drainage, intestinal suction, or enterostomy, free breathing, clean skin; avoid azotemia, toxemia, acidosis, and alkalosis.

5. *Contamination.*—Contamination may lead to infection. Antibiotics and chemotherapeutic agents should be given by mouth or parenterally.

6. *Early Mobilization.*—Early mobilization to avoid thrombosis and embolism.

7. *Environment.*—The patient should be kept warm not hot.

8. *Complications.*—Watch for the complications which cause shock. One of the best methods to discover shock early is to check the blood pressure and pulse every hour for the first twenty-four hours.

THE TREATMENT OF SHOCK

The studies which have been described have a very practical application in prevention and treatment. *In civilian life shock is encountered* most commonly from extensive wounds, burns, or fractures and after surgical operations. There is no way of preventing shock in the former; however, much can be accomplished in the way of prophylaxis in the latter.

whole blood or plasma or blood cells as required. Have enough blood on hand at all times to keep blood volume as nearly normal as possible. Use vitamin K.

3. *Water and Electrolytes and Food.*—Enough water must be given to meet ordinary needs but not too much. If there has been vomiting or diarrhea, enormous quantities may be needed. The ability to eat, drink, and assimilate food portends normal function. The alimentary canal and not the veins was made for those functions. In disease states normal channels may not be usable and the intravenous or subcutaneous routes must be employed; starvation states must be corrected before surgery (see Chapter 12). Vitamins must be supplied.

4. *Elimination.*—The ability to eliminate waste products, acid or base, is necessary for the avoidance of azotemia, toxemia, acidosis, and alkalosis. Therefore, interference with kidney or bowel function should be corrected if possible. Anuria may be avoided by attention to water, electrolyte, and colloid requirements if prerenal, or by drainage if postrenal. Bowel impairment due to obstruction may be relieved by tube suction or enterostomy.

5. *Ability to Withstand Infection.*—Chemotherapeutic agents and antibiotics make the environment unfavorable for bacterial growth.

During the Operation.—The most common causes for shock during surgery must be constantly borne in mind and avoided.

1. *Oxygen.*—Shock due to anesthetic agents is not common. It is usually anoxic anoxemia. This is avoided by a clear airway and liberal amounts of oxygen. Prolonged, deep anesthesia may cause shock during and after the operation—the former by affecting the respiratory and cardiac centers, the latter by prolonged lack of motion with pooling of blood.

2. *Blood.*—The surgeon must know the approximate amount of blood loss (see Chapter 14). He must avoid undue loss of blood by using accurate hemostasis, and he must replace that which he loses by transfusion during surgery. Therefore in all operations which ordinarily are accompanied by considerable blood loss, transfusions are started immediately after the operation begins. This is routine.

3. *Fluid and Electrolytes.*—Fluid and electrolytes are also replaced during surgery.

4. *Handling.*—Prolonged handling, roughness to gain time, prolonged exposure, even if tissues are handled gently, invite shock. Long procedures are better done in stages if this is feasible.

5. *Positions.*—The extreme Trendelenberg position and quick changes back to the horizontal after it has been employed may cause shock due to interference with the proper breathing and overloading the right heart while in the head-down position, and due to suddenly pooling blood in the abdomen when the horizontal position has been resumed.

6. *Environment.*—The patient should be kept at about room temperature—70° F.—warm not hot.

7. *Asepsis.*—Strict asepsis should be observed.

8. *Blockage of Afferent Nerve Impulses.*—There is no proof that blockage of afferent nerve impulses through the use of local or spinal anesthesia prevents shock.

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Once shock has occurred, an attempt should be made to diagnose its cause. Often this is very difficult, sometimes impossible. If we are able to diagnose the type of shock, this is of great value. Is it hematoggenous? If so, there is blood loss somewhere and this must be controlled. A brief reference to the causes of shock, as herein enumerated, will reveal immediately the complexity of the problem. However, if the different causes are kept in mind and if the patient is examined carefully, a diagnosis usually may be made.

While we are attempting to solve our problem as to cause, we must not neglect our patient lest he slip beyond our reach. One must not be so greatly concerned over the possible cause that he focuses his entire attention upon it and forgets that the patient is dying of shock. For in spite of the lack of diagnosis, the patient must be given adequate general treatment or he may succumb before the cause is found.

The Treatment of Neurogenic Shock

Since this type of shock is due to a pooling of blood, chiefly in the splanchnic area, the head down or at least a flat position is indicated. Tight clothing should be loosened; modest stimulation may be obtained by cold water to the face or the inhalation of aromatic spirits of ammonia. Carotid sinus syncope is helped by the foregoing measures and in addition atropine sulfate given hypodermically is indicated.

The Treatment of Traumatic Shock

In Chapter 13 we discussed the treatment of shock due to hemorrhage. Traumatic injuries include loss of whole blood, but in addition many other factors must be considered. Life cannot exist very long without oxygen or blood. Therefore our very *first consideration* in the management of severe injuries is to combat anoxia from whatever cause (see Chapter 19) and, no less important, to *control hemorrhage* or *the loss of plasma*. Every drop of blood counts. The same may be said of plasma. We have noted the effects of tourniquets on mangled extremities. Although they are often necessary, the rules for their use should be carefully followed (see Chapter 13). A tight pressure bandage is best until the bleeding vessel or vessels may be ligated or at least clamped. The use of cold to freeze a mangled extremity has been advocated because (1) it permits the use of a tourniquet for long periods due to the fact that it allows living tissue to survive on a low margin of blood supply; (2) it decreases the rate of autolysis; (3) it decreases the absorption of toxins (see Chapter 4). This is useful only if the extremity is to be amputated because such freezing not followed by amputation leads to gangrene or death from shock, infection, or both. If concealed bleeding is present, resuscitative measures must be instituted and the site of hemorrhage sought at the same time (Chapter 13). In burns plasma is held in the capillaries by external pressure or subcutaneous saline solution (see Chapter 4).

Rest.—The patient as well as his injured extremities must be put at *rest*. No matter what the cause of the injury, rest decreases pain and lessens exudation. For this reason temporary splints are important even though the trip to the hospital is a short one. Rest for the patient implies physical and mental rest. He should be kept quiet—for this purpose morphine may be necessary to relieve pain; a darkened, noiseless room to avoid any stimulation (shock room); and reassurance when consciousness occurs. Morphine is important but may increase anoxia by depression of the respiratory center. Therefore it should be used cautiously. This is especially true since it is usually given intravenously in shock. Drugs are not readily absorbed when given hypodermically, due to the peripheral vasoconstriction; consequently ¼, ½, ¾ Gm. may be given with little effect. As soon as blood volume has been partially restored, all of this will be absorbed at once, producing great respiratory depression even causing death. The "head down" position advocated by many is used with the idea that venous return to the heart will be facilitated. While this may be true, its disadvantages outweigh its advantages and therefore should not be used. This is clear enough in shock due to head injuries where blood should be pooled in the abdomen and in thoracic injuries where respiratory embarrassment may be increased. However, it is equally true that in abdominal injuries the diaphragm may be impeded by intra-abdominal bleeding or intestinal content or gas. At best this position leads to impaired breathing unless the air passage is clear so that an airway tube must be used in the unconscious patient, for any difficulty in respiration with a full right heart may lead to right-sided failure. Therefore the horizontal position is used except in shock due to head injuries or chest injuries, for which slight head elevation is indicated.

Restoration of Blood Volume.—Some fundamental axioms in restoring blood volume are (1) give that which has been lost; (2) take into account hydrostatic and osmotic pressures as well as the condition of capillary walls; (3) give fluid by mouth if possible; if not, use the intravenous route except with physiological saline which may be given subcutaneously with safety; (4) clinical symptoms and signs are the best guides as to adequacy of treatment.

In Chapters 12 and 13 we have discussed the various types of crystalloid and colloid solutions which are available for the restoration of blood volume, intercellular and intracellular water and electrolyte content. It should be borne in mind that (1) body fluids in blood and in interstitial and intracellular compartments form an isosmotic system in which semipermeable membranes maintain the solid content of the three phases with water transfer maintaining an equilibrium and a uniform osmotic pressure in all; (2) plasma is the most important part of the blood as regards its osmotic pressure because capillaries are normally relatively impermeable to the proteins it contains.

An enormous volume of literature has been written on the merits and demerits of the various solutions available in the treatment of shock. They fall into the following groups:

1. *Isotonic and Hypertonic Solutions.*—In the preceding paragraph we have noted that the fluid compartments are isosmotic. The great danger of hypertonic or concentrated solutions in patients who are in shock is that of dehydration, not only interstitial but intracellular as well. Also there is a direct stimulation of arterioles with more pooling in capillaries, although a transient rise in blood pressure occurs. Then, too, hypertonic solutions may cause kidney damage (see Chapter 12) and injury to vessel walls. Since a patient in shock may or may not have ample interstitial water, concentrated solutions are not as safe as isotonic solutions.

2. *Colloid and Crystalloids.*—Both are needed in shock. It is the sodium and potassium ions that are important, not only for osmotic reasons but also because sodium is lost into injured tissues where it may help neutralize toxins due to trauma. At any rate it must be replaced. Amounts equivalent to about 5 per cent of the body weight may be given parenterally during the first twenty-four hours. Saline cannot replace plasma but must be used with it because normally capillaries are permeable to crystalloids. If large volumes of saline are introduced, hydrostatic pressure is increased within the capillaries and osmotic pressure is reduced due to dilution; therefore, more fluid and plasma will be lost, thereby further reducing osmotic pressure. Those who favor saline over plasma aver that the loss of protein is due to local tissue breakdown, that plasma dilutes electrolytes which are vital, that glucose or plasma may stimulate metabolism, causing an increased tissue demand for oxygen. The latter is not true since protein and glucose are not synthesized during shock.

3. *Colloid Substitutes for Plasma.*—Gelatin, isinglass, pectin, methylcellulose, polyvinyl alcohol, vinyl pyrrolidon polymer—hydrophillic colloids, cause conglomeration and increased sedimentation of erythrocytes. Moreover, they do not furnish any material for the restoration of lost plasma protein and they may interfere with the formation of such proteins; they also may cause severe anemia due in part to their retention in the internal organs, especially the liver. Such inert materials should not be used when plasma is available.

4. *Amino Acids or Plasma Proteins.*—In Chapter 11 we discussed the use of protein solutions which are obtained from casein and pork pancreas or from casein alone as a source for amino acids. Such solutions used in concentrations of 5-10 per cent may be valuable when the liver is able to synthesize them into plasma proteins. In shock the liver does not function fully and therefore such synthesis is not available. Even if it were, the time element would preclude its use for an immediate source of plasma protein. Therefore plasma is much preferable.

5. *Whole blood, or Suspension of Red Blood Cells or Plasma or Albumin.*—These are the most needed and desirable remedies for shock.

Whole blood is always valuable in shock. This is true in cases where most of the blood volume loss is due to plasma. We have noted that in the treatment of burns, whole blood is useful even though there is hemoconcentration (see Chapter 6). The circulating hemoglobin may be rapidly reduced to one-fourth of the normal level with few symptoms, but a loss of approximately one-half the total blood volume is usually fatal. A million red blood cells per cubic millimeter can maintain life provided the circulating fluid volume is normal or nearly so. This is evident by the many patients who are brought into the hospital with erythrocyte counts of a million or even less. Of course the blood has been depleted slowly. Therefore it is fluid volume that is of immediate importance, although red blood cells are necessary to carry oxygen and anoxemia is one of the prime causes of shock. If there has been great blood loss or if there is a low hematocrit or *air hunger* (Chapter 19), whole blood is preferable. In the latter connection it is well to remember that cyanosis may be absent due to the fact that there is less than 5 Gm. of reduced hemoglobin in the circulation. Such patients will not be relieved by oxygen inhalation. They must have red blood cells.

Plasma will control shock even though it is due to hemorrhage because it will provide a medium to carry corpuscles, thereby decreasing anoxia; it may serve to mobilize red blood corpuscles sequestered in the various storehouses of the body such as the spleen and bone marrow and smaller vessels and actually lead to an increase in the blood count. Plasma is not a substitute for red blood cells, but it will tide over the critical patient and the erythrocytes will come later or may be given as *red blood cell suspension* in isotonic saline. The great value of plasma is that it is immediately available without typing and it fulfills all of the requirements for the maintenance of a blood volume compatible with life and physiological requirements (Chapters 11 and 13).

Serum albumin is, as we have noted in Chapter 11, the most important protein in plasma in the maintenance of osmotic pressure. Each gram of albumin should hold the equivalent of 18 c.c. of fluid in the circulation and a 5.6 per cent albumin solution should be isotonic with a 7 per cent plasma. Thus 25 Gm. of albumin is osmotically equivalent to 450 c.c. of circulating plasma or 500 c.c. of citrated plasma. During World War II a 25 Gm. package was available. Human serum albumin is very useful but difficult to obtain. It may be repeated at fifteen- to twenty-minute intervals, but when used in this concentrated form it is objectionable for reasons already given in the discussion of hypertonic solutions.

6. *Large or Small Transfusions.*—In hemorrhage where large amounts of blood have been lost a large quantity of blood must be replaced. This is particularly true during an operation where vessels may be ligated or

bleeding controlled by pressure. Where spontaneous arrest of hemorrhage is depended on, several small transfusions are preferable to one large one because of the sudden increase in blood pressure. This may actually precipitate further bleeding (Chapter 23). Shock due to trauma is also best treated by repeated small (500 c.c.) transfusions. This permits for vascular and other adjustments and precludes the possibility of shock from too much volume (plethora) with pulmonary edema or cardiac failure from overdilation. In addition, excessive amounts of whole blood lead to other serious complications such as intravascular thrombosis, stagnant anoxemia, anuria, and citrate poisoning which may lead to a fatality. Later complications include cerebral vascular accidents due to thrombosis or petechial hemorrhages and severe jaundice.

Use of Oxygen in Shock.—Oxygen is a subsidiary form of treatment in shock and when available it should be used. It is especially indicated in chest and head injuries. Oxygen is most effective when given under pressure. In anoxia free oxygen in the plasma must get to the cell which suffers not so much from lack of oxygen as from lowered tension (see Chapter 19).

Use of Heat or Cold.—Recently much has been written concerning the use of cold in almost all human ailments. In our *Synopsis of Principles of Surgery* we stated: "Keep the patient *warm*—surround him with hot water bottles and blankets." Notice we did not say keep the patient *hot*. In the beginning of this chapter we noted that peripheral vasoconstriction was necessary so that the vital centers could have a sufficient amount of blood and that perspiration is augmented so that body temperature may be lowered through evaporation, thereby reducing metabolism and the demand for oxygen in the presence of anoxemia. These we said were compensatory mechanisms. It is therefore wrong to cause peripheral vasodilation with external heat, defeating the provisions of nature's mechanisms, and moreover patients may be burned. Experimentally shocked animals live longer in cold than in heat and shock in very high environmental temperatures is more apt to be fatal than shock in cold, not freezing, temperatures. High temperatures decrease chance for life and shorten survival time in experimental animals, whereas cold lengthens survival time but does not increase the chance to survive. The fall in metabolism amounts to about 13 per cent for each degree centigrade that the body temperature is reduced. Subnormal temperature tends to prevent relative anoxia by diminishing the speed with which oxygen is used. The fall in temperature, as we have seen, is not the result of anoxia but is a protective mechanism, although anoxia does cause a fall in body temperature. A patient going into shock may feel warm; this is the converse of the chill which makes him feel cold. The former is a method for lowering body temperature, the latter for increasing it. The feeling of warmth like the sweat after a chill is to lower body temperature.

Those who are opposed to the use of cold in the treatment of shock aver that relatively little blood can be expressed from the skin because of peripheral vasoconstriction and that cooling of the body surface attended by a fall in body temperature of as little as 0.5 degree may induce shivering which would greatly increase the expenditure of energy and increase the blood flow through skeletal muscles. Furthermore, as the temperature of the body is reduced, hemoglobin holds oxygen more firmly, thereby aggravating the anoxemia that is present in shock.

Recent studies of recorded times of immersion of shipwreck survivors show that tolerance to water at temperatures below 68° F. is limited by the loss of body heat at a rate which exceeds heat production. Heat loss in water is twice that in air. In water, once the rectal temperature falls below 95° F., heat production decreases, respiratory and circulatory irregularities appear, and death ensues.

Lastly, if peripheral blood is cooled too rapidly, a slower circulation with increased stagnant anoxemia results. They believe that external heat as supplied by hot-water bottles and blankets cannot cause vasodilation and that if fluids are being administered it keeps the revived patient comfortable and is therefore useful.

It is undoubtedly true that extreme heat is harmful and that, in general, elevations of environmental temperatures cause more disastrous results than cold. A patient in shock is treated best by keeping him in an environment of 80 to 85° F., in other words, warm. It is indeed a far cry from extreme heat to allowing a patient struck by an automobile on a cold day to lie uncovered because he might force some blood to the surface. Hot-water bottles and blankets to keep him warm and dry is still good supplementary treatment for shock.

The Use of Drugs.—

Hypodermic injections of drugs are not readily absorbed due to the decrease in the circulating blood, to stasis, and to the flow of fluid and plasma into the tissues. Therefore, drugs are usually given intravenously. Caffeine sodium benzoate has been advocated and is useful for it increases blood flow and may improve stagnant anoxia. Adrenalin, ephedrine, and Tuamine sulfate have been advocated by some and condemned by others. Certainly the arterioles are constricted as much as possible in shock. More constriction or elevation of arterial pressure which does occur transiently simply causes more plasma to flow out of the dilated permeable capillaries, causing a prolonged lowering of blood pressure. In fact, a slow infusion of adrenalin may cause shocklike states to occur. Clinical experience bears out the logic of this contention. Even in the critical stage, where vasodilatation is present, adrenalin acts in a fleeting manner and although it temporarily causes an elevation of blood pressure (due to a temporary improvement of the coronary circulation and arteriolar vasoconstriction), this is followed by a more pronounced and prolonged fall in blood pressure. Vasoconstrictor

drugs like adrenalin are useful in shock due to (1) spinal anesthesia, (2) spinal trauma, (3) anaphylaxis, and (4) histamine. In the first two it acts upon the dilated arterioles; in anaphylaxis its action is not definitely known but bronchiolar spasm is lessened. In histamine shock the arterioles are dilated. Adrenocortical hormone (eschatin) does not prevent shock when used preoperatively but is said to decrease capillary permeability in shock. Experimental and clinical experience indicates that plasma is not better retained with than without it. (See Chapter 22.)

Attend to the injury which has brought on the shock after resuscitation is complete; that is, if a mangled leg is the cause, it may now be treated in accordance with sound surgical principles.

Surgical operations should not be done with a patient in profound shock. In all injuries external bleeding is controlled first; then measures are taken to replace blood volume. Internal injuries are divided into two classes: those associated with great blood loss and those without. In the former large quantities of blood are given and operation is done as indicated, as soon as there is fair reaction. Blood is given during and after the operation as well. In ruptured ectopic pregnancy with hemorrhage, or bleeding duodenal ulcer (despite recent advice to the contrary), if resuscitation cannot be obtained, at least partially, an operation should not be attempted. Natural arrest of bleeding will occur in most cases, and after reaction is complete surgery may be done much more safely. In ruptured viscera without massive hemorrhage, reaction from shock is obtained before surgery. This is usually accomplished within 1 to 2 hours.

The Treatment of Cardiogenic Shock

The surgeon may see this form of shock during an operation. Manual massage through the diaphragm may result in a return of regular cardiac contraction. This occurred during an operation by the author for carcinoma of the lower esophagus. Resection was complete when suddenly the heart stopped. Cardiac massage was carried out for two minutes before feeble contractions were resumed; 1,000 c.c. of whole blood were given during the procedure and 500 c.c. more were started. Fifty milligrams of procaine hydrochloride were injected into the left ventricular cavity. This was repeated in two minutes. After this the contractions were normal. The patient recovered and is still well four years later. Some recommend the injection of adrenalin directly into the heart muscle, 1 c.c. of a 1:1000 solution. (See Chapter 17.) For coronary thrombosis the relief of pain is paramount. The best drugs are morphine, 0.015 Gm. (1/4 grain) intravenously, or 100 mg. of Demerol, hydrochloride, or papaverine, 0.03 to 0.1 Gm., intravenously. Complete rest and oxygen by inhalation are important adjuncts to treatment. Fluid balance must be maintained, and for this purpose isotonic saline by hypodermoclysis is best.

This route is chosen because it supports the distended veins by increasing *intercellular space pressure and it will be absorbed more slowly, thereby* avoiding an overload on the heart. (See Chapter 11.)

The Treatment of Toxemic Shock

We have seen that extensive burns produce shock. The same effect is noted when inflammations of the skin arise from other causes such as severe dermatitis, cellulitis, gas gangrene, etc. Since the peritoneum is equal to the skin surface, inflammations involving a large part of the peritoneum are also likely to cause shock. The toxemia is partly bacterial but also may be due to other factors as discussed in Chapter 6 under Burns, in this chapter under Traumatic Shock, and in Chapter 4 under Diffuse Inflammations.

The treament is the same as that for traumatic shock with a few additions and modifications. Fresh blood or fresh plasma is desirable because *of its high antibody titer. Antibiotics and chemotherapeutic* agents are necessary. In tetanus and diphtheria antitoxin is indicated.

Treatment in Special Types of Shock

Thoracic.—Shock may occur following thoracic injuries or operations just as in other parts, and its prevention and treatment has been described. There is, however, a type of shock which resembles ordinary shock but which is peculiar to chest operations and injuries. The chief causes of this type of shock have been discussed. The treatment will be discussed again in Chapter 19. A brief summary is included here.

A "sucking" wound of the chest must be plugged immediately, using petrolatum gauze, dry gauze with adhesive, the hand, or anything which is available. In the hospital it will be sutured. Tension pneumothorax is relieved by inserting an aspirating needle in the second or third *intercostal space anteriorly in the nipple line. Air will escape* under pressure. If this continues a slit finger cot, or the finger of a rubber glove slit at the end may be tied to the hub of the needle which is anchored to the chest wall by adhesive. In this way air can get out but not in. Or a tube may be attached to the needle and placed under water, permitting the exit of air or fluid but *not its entrance.*

Postoperative shock following thoracic operations (see Chapter 19) is treated by replacing blood volume and giving oxygen by inhalation. Parodoxic respiratory movement is prevented by not removing too many ribs at one time in thoracoplasty. It is treated by placing a firm pressure *dressing over the area of paradoxic* movement, an inflated rubber vest, allowing the patient to lie on the area, aiding him to evacuate retained pulmonary secretions (q.v.) so that dyspnea will be reduced and therefore the paradoxical movement lessened; in severe cases the Drinker respirator may be used. Air and fluid must be aspirated from the pleural cavity *if it accumulates under tension.* To prevent this, air-tight closure

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Blast Concussion and Immersion Blast.—The treatment of blast concussion is first that of traumatic shock; then it is largely governed by individual indications. Usually it is symptomatic. If extensive hemorrhage or laceration of solid or hollow viscera is evident, surgery is necessary.

Acceleration shock rarely occurs from accelerations in the transverse axis of the body. With positive acceleration if blood could be kept from leaving the head and chest, ill effects could be overcome. Tensing the abdominal muscles, as in screaming, is of some value. An abdominal belt inflated to a pressure of about 75 mm. Hg for one-half minute before exposure to the expected acceleration increases acceleration tolerance by 2 to 3 "G's."

Environmental Temperature.—Overheating or heat exhaustion is rarely serious. Treatment consists of placing the patient in a cool place out of the sun, loosening tight clothing, and stimulation by cold water to the face or inhalation of aromatic spirits of ammonia.

Sunstroke or heat retention is serious and requires attention to water and salt metabolism, cool environment, rest, and external application of cool moist cloths. Since body temperature is lost by evaporation, convection, and conduction, all methods are utilized. The best results are obtained by the application of cold moist towels for thirty minutes and then their removal; the air is kept in motion by electric fans directed away from the patient. By this method the skin is cooled and thereby the peripheral blood. Then when vasoconstriction occurs the cold is removed, allowing blood to return to the surface for cooling which is augmented by the evaporation of surface water.

Shock from prolonged exposure to cold is best treated by rapid warming. This is obtained by merely placing the patient at rest in a warm room. Attention to water balance, nutrition, and blood volume is necessary.

Irreversible Shock.—Irreversible shock is a type that should be discovered by failure of treatment. In other words, no patient should be considered in irreversible shock regardless of time element, cause, or other factors. Every surgeon has seen the apparently "hopeless" case respond to vigorous scientific treatment and then go on to recovery. Even anoxia of five minutes or more may be followed by recovery, albeit often with a damaged cerebral cortex. There is no test which brands shock as irreversible, and even if there were the good physician would supply the patient with blood and oxygen in the hope that all tests may fail.

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of the pleura and chest wall is necessary. Closed drainage is used by introducing a small catheter which is sealed to the chest and is connected by a glass adapter and soft rubber tube to an under-water seal. Evacuation of pulmonary secretion and blood is extremely important. Following the operation the anesthetist must aspirate secretions through the endotracheal tube; then bronchoscopy is done to suck out all portions of the bronchial tree. Until the patient is awake, he should be in the Trendelenburg position, 10 to 15 degrees. As soon as consciousness returns, the patient is allowed to sit up, his chest held by the nurse, and allowed to cough up retained secretions. Sometimes a catheter attached to a suction machine must be used to facilitate the removal of thick ropy mucus and old blood from the pharynx and upper trachea. Heavy doses of narcotics should not be given and the patient should sleep on the affected side. Oxygen should be discontinued as soon as possible.

Cardiac tamponade due to stab or bullet wounds of the heart demands immediate surgery with blood started slowly in an attempt to produce a reaction from shock. If blood is given too rapidly, and this can only be done if given under pressure or intra-arterially because of the high venous pressure, shock may be increased due to more blood in the pericardium. As soon as the pericardial sac is opened, shock is lessened; blood is given while the lesions are being repaired. Shock due to the accumulation of fluid from pericarditis is less severe and may be treated by aspirations or drainage.

Crush or Compression Syndrome.—The treatment of compression syndrome resembles closely the treatment of extensive burns. Since renal failure is the usual cause of death, the establishment of an alkaline diuresis is desirable. If the patient can swallow, large doses of sodium bicarbonate should be given (4 Gm. per hour until the urine is alkaline; then 30 Gm. per day for two days). Should vomiting preclude oral administration, 1 liter of isotonic sodium lactate (one-sixth molar = 2 Gm. per 100 c.c.) may be given intravenously, or sodium bicarbonate, 3.5 Gm., as available in sterile ampoule for intravenous use. An average of 3,000 c.c. of fluid should be given per day in the adult. This may be administered by hypodermoclysis into the injured area if the patient is unable to swallow.

Local treatment consists of pressure bandage or surgical intervention after reaction from shock. That is, if compression has produced gangrene, amputation may be necessary in an extremity, or local excision of necrotic areas may facilitate healing and delimit toxic effects. Shock is treated by restoration of blood volume with whole blood, plasma, or both. Anuria may occur in spite of treatment and therefore a close watch is maintained of urinary output. With established renal failure fluids must be restricted and here plasma or glucose solution, 5 per cent, is more useful than saline. The danger in patients with anuria is overhydration and pulmonary edema. Hypodermoclysis is safer than intravenous administration. (See Chapter 23 under Anuria.)

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PART IV

REACTIONS OF TISSUES AND ORGANS TO TRAUMA OF UNKNOWN ORIGIN

Chapter 15

TUMORS AND CYSTS

Previous chapters have dealt with the reactions of different tissues to injuries of all kinds. We learned about repair following injuries which result from mechanical forces and bacterial invasion. Next we considered the reasons for delayed healing or lack of repair or destruction of tissue in the chapter on Ulcer and Gangrene. Miscellaneous bacterial causes for injury and the more or less characteristic type of reactions to such trauma were then reviewed. Lastly the behavior of the entire organism in its reponse to trauma which has widespread effects was discussed in the chapters on The Human Constitution, The Interchange of Body Fluids, Acid-Base Balance, Hemorrhage, and Shock. In this section of the book we are again endeavoring to describe the body's reaction to trauma. Unlike previous descriptions we are unable to name the cause of the injury, although its morphological and to some extent its biochemical and physiological effects are known. It follows, since we do not know all of the cause or causes nor the full effects of the injury, that prevention and treatment must rest entirely on empirical ground.

The body fights its adversaries with increased blood supply and cells—blood is the "life line" of fighting forces and cells are the fighters. Cells engulf, surround, erect fences (fibrous tissue) and block all roads (lymphatics and capillaries) which may lead to the escape of the enemy. Even in this weird, devastating and morbid process called neoplasia, the body fights back, and in the light of recent experiments this fight is beginning to be partially understood.

New growths were known to the ancients and are mentioned in Papyrus Ebers (1500 B.C.). The ancients treated them by excision and by escharotics, such as arsenical ointment. The latter were *temporarily* abandoned but have recently been revived. They may not completely remove the growth, but they do not spread it. The word cancer was originally used by Herodotus to mean any chronic growth or swelling. Hippocrates (460-375 B.C.) burnt out a carcinoma of the neck—the earliest record of diathermy. Neoplasms are widely disseminated in nature (lower animals, plants, trees) and are more common in civilized than in uncivilized peoples.

The word *tumor* means a swelling and though it might from its derivation be applied to inflammatory lesions, it is ordinarly used today to re-

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duct of a gland. (Cysts will be discussed in one of the following paragraphs.) These swellings, with a few exceptions (such as cystadenoma), *are not neoplasms. Hypertrophy means an enlargement of the cell; hyperplasia* means the production of new cells. Simple epithelium when irritated may undergo metaplasia, becoming stratified. This is seen in the ciliated epithelium of the bronchi in chronic infections and of the uterus. Although the increase in the number or size of the cells results in an enlargement of the organ involved, the process in either case serves a useful purpose and is initiated because of an increased demand upon its function. It is governed by the normal physiological laws of growth. Thus, an adenoma may be the result of an attempt at hyperplasia and hypertrophy with subsequent fibrosis about the area as seen in the breast and thyroid.

Invasion and destruction of tissue is a characteristic of cancer. However, it is true that leucocytes invade tissues and so do the so-called trophoblasts in the early stages of pregnancy invade the body of the uterus. Unlike cancer, these cells when "mature" are sloughed and the uterine wall is restored to normal unless a cancerous process, chorio-epithelioma, supervenes.

Cancer is a process in which certain cells in an organized cell group become "wild," resembling early embryonic tissue morphologically, immunologically, and biochemically. But unlike normal embryonic tissue, differentiation does not occur; moreover, heterologous transplants of embryonic tissue may be successfully made up to the fifth month of *gestation. The same property exists in many cancers.*

TUMORS

Structural Characteristics of Neoplasms

New growths are spoken of as *histioid* or *organoid* in structure: histioid growths are composed of cells (for example, a lipoma or fatty tumor is *made up of fat cells*); *organoid growths are composed of organs (an* hemangioma is made up of capillaries; a dermoid tumor may contain teeth or hair; a teratoma contains fetal remains). The term *lepidic* refers to a growth in which the cells lie next to each other, as in epithelium or endothelium. *Hylic* growths contain cells separated by a matrix, as in connective tissue or bone. *Homologous* growths are those in which the tissue is like the organ in which they are growing, whereas *heterologous* growths are those in which an unlike or mixed type of tissue is encountered. An example of the latter would be a chondroma (a cartilaginous growth) found in glandular tissue; for example, in the breast or the parotid gland. New Growths may be *encapsulated,* in which case they are apt to be benign, or they may be infiltrative, in which case they are apt to be malignant. *Unicentric* growths have one place of origin; occasionally neoplasms are *multicentric,* as in the colon, with two or three points of

fer to new growths and cysts. The word *cancer* is commonly used to imply a malignant growth. *Neoplasm* means new growth, and *neoplasia* means the formation of new tissue. As the terms are usually employed, they mean that the new tissue is abnormal as to anatomy and physiology.

A new growth may be suspected in the case of any swelling which exists where it should not be or in the case of any chronic ulcer that does not heal according to the normal laws of repair. On the outside of the body this is easy to detect. In the internal organs we must depend on the history and symptoms, signs, a study of transudates, exudates and secretions for deciduous cells, x-rays, and endoscopy to help us. There are as many different kinds of new growths as there are different kinds of cells that occur in the body or in embryologic development. Therefore, neoplasms constitute a heterogenous group of anatomic defects which are as numerous as the different kinds of tissue.

We have said that repair is an orderly purposeful attempt on the part of nature to heal or to reconstruct continuity of tissue, both as to structure and, in some cases, as to function. The neoplasm, unlike repair tissue, has an independent character of development. This has been called *autonomy* or *self-determination* and is not fully understood, but it manifests itself in an *excess proliferation of tissue* or tissues which has no natural termination and serves no purpose. Although many normal cells cultivated in vitro possess autonomy, they lose this property when implanted in the animal body. When a new growth occurs in an endocrine gland the gland is sometimes stimulated to perverted activity or overactivity, as in pituitary adenoma (Cushing's disease) or parathyroid adenoma (hyperparathyroidism). Neoplasia is harmful to the general body economy and has no useful function. It acts like a parasite in that it derives its nourishment from the blood supply of the host and lives at his expense, but cancer cells are not supplied with nerves from the host. However, so far as is known, new growths are not parasitic in origin, although they are known to arise in tissues which have been the site of parasitic infection. In order to illustrate this point more clearly, we may give examples of other swellings which are not neoplastic.

Many infections produce tumorlike lumps such as *warts* and *condylomas* (flat growths usually associated with venereal infections); although these lumps may not have a useful function, yet they are classed as defensive inflammatory reactions to infection, which is not true of new growths. Epithelial cells have no other inherent method of defense except hypertrophy and hyperplasia. Condyloma accuminata are called forth by any irritation, whereas condyloma lata are due to syphilis. The former are thought to result from a virus. *Gigantism* is also excessive growth of tissue, but it is normal in architecture and in cellular content; therefore, the sum total of tissue is larger and greater, but it does not come under our classification of neoplasms. *Cysts* may be inflammatory in origin but are usually due to an obstruction of the principal

duct of a gland. (Cysts will be discussed in one of the following paragraphs.) These swellings, with a few exceptions (such as cystadenoma), are not neoplasms. *Hypertrophy* means an enlargement of the cell; *hyperplasia* means the production of new cells. Simple epithelium when irritated may undergo metaplasia, becoming stratified. This is seen in the ciliated epithelium of the bronchi in chronic infections and of the uterus. Although the increase in the number or size of the cells results in an enlargement of the organ involved, the process in either case serves a useful purpose and is initiated because of an increased demand upon its function. It is governed by the normal physiological laws of growth. Thus, an adenoma may be the result of an attempt at hyperplasia and hypertrophy with subsequent fibrosis about the area as seen in the breast and thyroid.

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growth occurring simultaneously. Although the latter are usually benign, multiplicity of origin is seen in malignant growths as well. These may be in the same organ or in paired organs or in widely separated areas.

Manner of Growth.—Tumor cells multiply by mitotic division or by amitosis, or direct division may occur, but if so it is rare.

A. *Expansive* growth is characteristic of benign neoplasms. As they grow they push aside the adjacent tissue. (Lipoma, fibroadenoma, etc.)

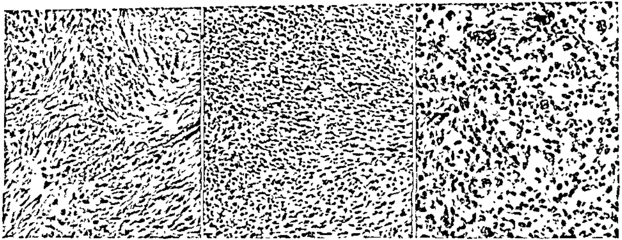
B. *Central* growth progresses in a centripetal manner; in other words, the oldest tissue is that around the edge (fibromyoma, etc.). Growths by expansion of the original mass follow this plan of growing principally in the center of the tumor; therefore, A and B usually go together.

C. In *peripheral* growth the actively growing cells are around the periphery. This may be termed a centrifugal type of growth, with the oldest tissue in the center. This makes eradication more difficult. It is sometimes seen in benign tumors (chondroma), but is usually a characteristic of malignant neoplasms.

D. *Extensive* growth extends or spreads to contiguous tissues without complete involvement of intervening structures. (Proliferating papillary cystadenoma and Krukenberg tumor.)

E. *Infiltrative* growth spreads and invades adjacent tissues and structures, as in carcinoma of the cervix, where first the entire cervix, then the ureters, the bladder, and the broad ligaments are invaded. Thus neoplastic buds or projections enlarge, fuse, and destroy intervening tissue, including blood and lymph vessels, thereby providing for their dissemination. Infiltration may be due to pressure, interference with blood supply, or infection. A tumor may look hopeless at operation, but microscopic studies may show infiltration which is not due to neoplastic cells but rather to inflammation, and the enlarged lymph nodes may also be inflammatory rather than malignant.

Character of the Cells.—Neoplastic cells may resemble normal cells or they may resemble their primitive forebears; namely, cells of the embryological tissue from which they are derived. The more nearly a neoplasm resembles normal tissue, the less malignant it is, and the contrary is true. Some have based their diagnosis as to malignancy on this fact. This has been called Broder's classification. If the majority of the neoplastic cells in a growth resemble the normal, the growth has been called type I, whereas in those growths in which the majority of the cells are definitely embryonic in type, the growth has been called type IV. Types II and III are intermediate between I and IV. Dukes' classification is useful in neoplasms of the large intestine and is based upon the degree of invasion. In type A the growth is limited to the wall of the intestine. In type B it has extended to the outside and has involved extracolic or extrarectal tissue. In type C the growth has spread to ad-



A. B. C.

Fig. 110.—Spindle-cell sarcoma; fibroblastic sarcoma. *A*. Low grade of malignancy. Cells are of the adult type; cell fibrils are abundant (fibrosarcoma). *B*. Moderate degree of malignancy. There is increased cellularity with less intercellular substance. The cells are much smaller than normal fibroblasts (small spindle cells). *C*. Highly malignant large spindle-cell sarcoma. The loosely arranged cells are atypical in size, shape, and staining reaction. Note malignant giant cells at the top.

jacent lymph nodes. A fourth type, D, would include metastasis to the liver. Neoplasms are also spoken of as *more* or *less* atypical in structure or arrangement, the former being malignant, the latter tending to be benign.

Neoplastic tissue is made of *cells* and *stroma*. The latter makes up the framework and carries the blood supply. This comes from the host and is commandeered by the neoplasm.

Neoplastic cells are usually round and have more deeply staining nuclei than normal cells. Their function is abnormal in respect to the production of fibers, matrix, or secretion. However, some of the less malignant do have a primitive function, such as the production of mucous (mucus adenocarcinoma) or the production of bone (osteogenetic sarcoma). We may readily deduce that these latter types of growth are apt to be less malignant than those which destroy rather than produce a secretion or substance, however, primitive the secretion may be. That is to say, if the neoplasm produces any form of secretion or tissue, it approaches the adult as distinguished from the embryonic type. Sometimes epithelial cells are displaced due to attempts at repair, into a new environment. Thus buried epithelial cells are seen in chronic ulcers of the leg, etc. In the colon these cells are found in the submucosa as isolated groups which may form a cyst or a neoplasm due to their altered environment. Such cells may therefore vary from normal to widely aberrant epithelial cells.

The word *anaplasia* has been used to describe the primitive type of cell and means a reversion to the embryonic state (*ana*, against; *plasia*, growth).

The word *dedifferentiation* has been used to mean the same thing. The thought that this word conveys is that instead of a cell's growing from its primitive embryonic form into an adult cell, it does exactly the opposite: it "dedifferentiates" into its primitive forebear. Most observers agree that mammalian cancer cells are derived from normal cells. Ewing states:

> Striking peculiarities in such a fundamental process as cell division may well *suggest that here is disclosed the essential nature of tumor growth.* Hansemann has interpreted the studies in this field in such a manner, holding that asymmetrical, multipolar and abortive mitoses mean unequal distribution of cell potencies, loss of cell differentiation, freedom from normal restrains to growth, and exaggeration of *growth* over functional capacities. These physiological properties he included in the conception of *anaplasia,* the morphological side of which is illustrated in resting and dividing tumor cells.

The majority of tumor cells, according to Ewing, divide by normal mitosis: abnormal mitoses are secondary results of tumor growth.

Malignancy and Benignancy.—*A benign or "innocent"* growth is one that is encapsulated and is therefore freely movable in the tissue. Its cells resemble the normal, and the tumors are usually multiple. Growth is

Fig. 111.—Papilloma. The epithelium shows a great amount of infolding but there is no penetration of the basement membrane.

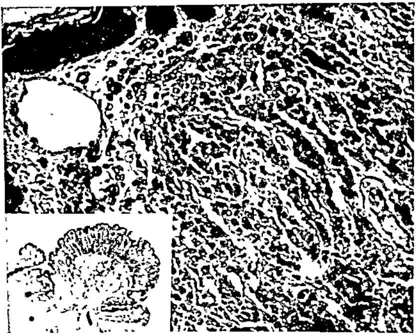


Fig. 112.—Papillary nevus (elevated pigmented mole). The low power shows the lack of invasiveness indicating its benign nature. The high power shows the chromatophore cells. Nerves are also seen. These tumors are frequently found in von Recklinghausen's disease.

extremely slow (months or years), and if death should ensue it would be caused by the interference of the growth with some vital function due to its location and size rather than to a destruction of tissue. An example of this would be a benign growth in the brain or in the esophagus or bronchus.

A malignant growth is usually, though by no means invariably, single; its growth is rapid (weeks or months); it is fixed in the tissue because of its infiltrative growth. It often degenerates and ulcerates, and it may spread to other parts of the body. Hemorrhage and disturbance of function are common, and in its later stage a state of disability, known as cachexia, ensues. Such a growth is apt to recur after being removed unless the removal is thorough, complete, and early. There is generally no capsule and the growth may be very vascular and meaty. Areas of hemorrhage and necrosis are encountered, and the edge shades off into the surrounding tissue. Bleeding is an early symptom due to friability.

Under the microscope we see, first, cells—cells everywhere—with little or no stroma; dedifferentiation cells (anaplasia), with variation in size, shape, and staining reactions; a very few thin-walled blood vessels; and the inclusion of fragments of surrounding tissue (showing the growth's infiltrative character). Evidence of rapid growth is found in the mitotic figures that are encountered. (These occur in cells in which the nucleus is dividing.) In other words, the growth is abnormal in respect both to the cells and their architectural arrangement.

On the basis of his experience with over 50,000 neoplasms, MacCarty recognizes three great groups: (1) those neoplasms composed of adult cells, with normal tissue arrangement; (2) those composed of cells normally, or nearly normally, arranged but having the morphology of malignant, regenerative cells; and (3) those composed of cells of the malignant, regenerative type, not arranged in any fashion approaching that of any normal tissue. Clinical experience has shown that neoplasms of the first group are not invasive and do not metastasize. They interfere with the function of the organ or tissue containing them and sometimes, by their extensive growth, interfere with neighboring structures. They are spoken of as being clinically benign, although they not infrequently kill their host, and are, therefore, in a sense, just as malignant as groups 2 and 3. Such terms as adenoma, osteoma, neuroma, myoma, and chondroma have been applied to tumors in this first group. The second and third groups embrace the so-called clinically malignant tumors, the adjective "malignant" usually connoting invasion of normal tissues by the new cells and migration of the new cells to other parts of the body, thus forming metastases. From a practical standpoint there is no great clinical difference between group 2 and group 3. Both are malignant and both kill the host. The only differences are the histological pictures and the usual greater malignancy of group 3. The therapy for the two

groups is the same. Transformation of a benign to a malignant growth may occur in rare instances, as in congenital polyposis of the colon. It is generally agreed, however, that there is less chance of a malignant growth developing in a benign tumor than there is of a malignant tumor growing in an area not previously tumorous.

The word *metastasis* is of Greek derivation. *Meta* means "in the midst of," and *stasis* means "a placing." As commonly used, it means the dissemination of neoplastic cells into different portions of the body. This may occur in two ways: (1) by way of the lymphatics and (2) by the blood stream.

Fig. 113.—Neurofibromatosis (von Recklinghausen's disease).

Lymph metastasis is usually encountered in carcinoma (malignant epithelial growths). It may take place in two ways: by embolism or by permeation. (1) *Embolism* refers to a cell's or groups of cells' breaking off and being carried by the lymph vessels to the anatomically related lymph nodes. Since the lymph channels enter the lymph node peripherally, through the cortex, such cells will be found in the cortical portion. An example of this type of metastasis is epidermoid carcinoma of the lower lip, where cells do not involve the chin but deposit themselves in the submental lymph nodes. (2) *Permeation* is a process which has been made clear by the work of Sampson Handley. (Chapter 16, Carcinoma of the Breast.) The cells grow along the wall of the lymph channel and by retrogressive growth infiltrate the superficial lymphatics of the surrounding tissues, the reticular lymph vessels as well as the tubular. This permeation is carried along the deep fascia upon which the tubular lymphatics lie, finally involving the lymph nodes. This per-

meation causes a *perilymphatic fibrosis* (Chapter 17). The process has been compared to the spread of a prairie fire, whereas embolism is like the flight of a bullet. Small lymph vessels are easily plugged by cancer cells which break through, causing perilymphatic fibrosis. Large lymph vessels carry groups of cells as a unit—that is, as emboli. Carcinoma of the breast spreads by permeation (Chapter 16). It is easy to understand that in metastasis by embolism the surgeon would be required to remove the primary growth and the lymph nodes involved, whereas in metastasis by permeation he would be required to remove the growth and in addition a wide area of skin and all intervening fascia (on which the lymphatics lie) as well as the lymph nodes involved.

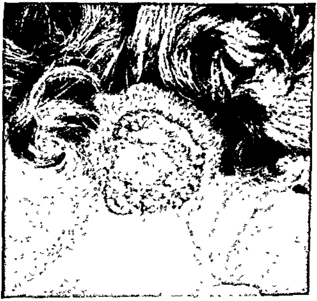


Fig. 114.—Squamous-cell carcinoma of the neck. Note the elevated margin.

Blood stream metastasis is more commonly encountered in sarcoma (connective tissue malignancy) than in carcinoma. Here a group of cells breaks off after penetrating the thin-walled veins and is carried quickly to the lungs. If a sarcoma has metastasized, it is hopeless. No matter how thorough the surgery may be, cure will be impossible unless some new carcinotoxic agent is forthcoming. Such neoplasms as those of the thyroid and testis and malignant melanoma or lymphosarcoma metastasize in both ways. These are particularly malignant. The surgeon should always look for metastatic growths before operation is attempted. Such growths may be found upon x-ray of the lungs and bones or palpation for "sentinel" nodes in the supraclavicular region. Metastatic masses may be found in the pararectal fossae (Blumer's shelf), the pouch of Douglas, or the umbilicus. An enlarged liver (nodular) with ascites may be discovered.

Malignant neoplasms may metastasize also in peculiar and bizarre combinations of ways. The coelomic cavity is frequently invaded by can-

cer which originates in the lungs, bronchi, or gastrointestinal tract and also by malignant growths outside the thorax or abdomen such as cancer of the breast. The pleura and peritoneum have very little capacity to arrest cancer; hence once invasion has occurred the malignant process spreads rapidly. Intrapericardial invasion is usually by direct extension from the lungs, bronchi, or breast. The cerebrospinal spaces are invaded by carcinoma of the breast and may spread throughout this area resembling a cerebrospinal meningitis in symptomatology. Invasion of the blood stream is common for sarcomas, but their involvement of lymphatics is rare except in lymphosarcoma. This is probably due to the greater local fixation of sarcoma cells as compared with the mobile and sometimes ameboid cancer cell (Ewing). This is the reason that lymphosarcomas behave much like carcinomas. Also, sarcomas are more vascular than carcinomas so that cells may invade and break into the thin-walled blood vessels. Finally the growth of sarcomas is more expansive and encapsulated so that lymph vessels are closed but nutrient blood vessels are open. The invasion of the blood stream may occur by the following avenues:

1. Direct involvement of vessels by primary or secondary tumors.
2. Secondary embolism; that is, emboli arrested in the lung may grow through the vessels and break into the pulmonary veins.
3. Tertiary embolism; that is, metastatic tumors in the liver, producing pulmonary emboli.
4. Retrograde transport as distinguished from Handley's permeation theory means that emboli actually travel against the blood or lymph current. Retrograde transport occurs chiefly in those organs with a normal venous pulse (lungs, liver, kidneys, heart, and brain) and in which violent changes in intrathoracic pressure may transform the weak forward into a backward current. When the main lymph or blood channel is occluded, backward transport may occur more commonly in the latter, although collaterals should prevent this. Retrograde metastases may start from tumors within or without the organ involved. Examples: a large tumor thrombus from primary sarcoma of the tibia lying in an arched vein of the kidney could originate only by backward passage through the renal vein of an embolus traveling from below; emboli in a cerebral sinus with cancer of the breast, in an hepatic vein from intestinal or thyroid cancer, and in cerebral, cardiac pulmonary and hepatic veins in hypernephroma; through the lymphatics—bronchial nodes with subpleural lymphatic invasion but without pulmonary parenchyma involvement; gastric carcinoma with involvement of portal, lumbar, and inguinal nodes may be retrograde or by permeation.
5. Paradoxic embolism by way of a patent foramen ovale.
6. Passage of single cells through pulmonary venules.
7. Through the thoracic and right lymphatic ducts.

Metastasis of benign tumors is probably a misnomer. However, it is seen in metastasizing "adenomas" of the thyroid. Such growths may invade surrounding tissues so that extirpation is as impossible as in late carcinoma of the thyroid. Yet the microscopic studies show "fetal adenomas" and adenomatosis with hyperplasia and great vascularity. We are not sure that these are benign "adenomas." Bronchial adenomas, chondromas (these may come from a teratoma not so recognized) and leiomyoma of uterus are usually listed as benign growths. However, the element of malignancy is difficult to rule out in these tumors, particularly the bronchial adenomas.

Fig. 115.—Squamous-cell carcinoma (prickle-cell cancer) of the finger. The low power shows the ulcer and the invasive character of the growth. The high power shows epithelial pearl and malignant cells. Note the intercellular bridges.

Some general observations on metastases are:

1. Most squamous carcinomas of the head and neck spread to the cervical lymph nodes but rarely below the clavicle. Practically none show distant metastasis without first having cervical node involvement.

2. Distant metastases from cancer in the upper respiratory and alimentary tract, due to blood-borne metastases occur in about 23 per cent. The most common sites are lungs, liver, and pleura in the order named.

3. Patients with cancer of the mucosa of the cheek, gingiva, palate, nasal cavity, and esophagus show the greatest incidence of systemic dissemination of primary lesion.

4. The morphology of the tumor gives no hint as to the probability of distant metastases but the age does. The younger patients show the greatest tendency.

5. Supraclavicular lymph node involvement from abdominal and thoracic cancers is uncommon. The sentinel or Virchow node is not often affected. When it does occur it is more frequent on the left than on the right where it occurs mainly in patients with thoracic cancer. Both supraclaviculars are involved still more rarely and practically always from thoracic malignancies. Although these nodes may be the *first* clinical signs of thoracic or abdominal cancer, in most cases generalized metastases have already occurred at the time that the cervical nodes are involved.

6. Lymph node involvement may be the first and only symptom of cancer. We have seen this in cervical nodes especially in cancer of nasopharynx, axillary nodes in scirrhus carcinoma of the breast, inguinal nodes in carcinoma of anus and vagina.

7. Every swelling in the neck, axilla, or inguinal region must be considered seriously as a probable tumor enlargement due to metastatic node involvement. Although primary growths and node involvement due to other causes must be considered (Chapter 17), the fact that the swelling is a metastatic node must be kept in mind. An accurate knowledge of anatomical node arrangement, a careful history, and repeated examinations may reveal the hidden cancer. Biopsy should be reserved for the last, not the first, means of diagnosis.

Theories as to the Cause of New Growths

The cause or causes of new growth are not known. However, it is correct to assume that as in other surreptitious invaders, it takes two to make the bargain—The carcinogenic factor and the resistance or lack of resistance of the host. Ewing spoke of the *causal* genesis of tumors including the inciting agents leading up to the development of malignancy and the *formal* genesis or the factors responsible for the nature of the cancer cell and its tendency to autonomy. These two factors, the remote extrinsic or contributory and the proximate intrinsic or actual causes, constitute as in all diseases the problem of carcinogenesis. Let us first consider some of the older concepts and then the more modern interpretations of the cause of neoplasia. At the outset we must remember that much of the recent work is being done on experimental animals and since there is great variation in susceptibility and behavior of different lower animal groups and species there obviously may be a great difference between the findings in mice and the effect on man. In this review we shall attempt to integrate these findings wherever possible.

Cohnheim spoke of *cell rests*, by which he meant the enclosing in normal tissue of a group of embryonic cells which may suddenly take on new growth. We may liken this to a new building in which brick and mortar may be mislaid in various areas during construction. This explains the structure of such growths as dermoids and teratomas, but we are totally unable to explain why the misplaced cells suddenly take on wild and unlimited growth.

Ribbert believed that one component (the cells) grows because the other (the stroma) does not restrain. Little has recently reaffirmed this theory stating that carcinogenic agents act by removing inhibitory influences to cell growth and production. Thiersch said connective tissue fails as old age approaches. Some observers aver that neoplasia is "repair gone wrong." It starts as normal repair and does not have the restraining influence necessary to stop proliferation. Waldeyer believed that *connective tissue grows rapidly and aberrantly and irritates epithelium* into activity.

Genetic Factors.—One of the most important studies on the cause of cancer is the role played by hereditary transmission, or inherent predisposition to the disease. Does the formal proximate intrinsic or actual cause of neoplasia reside in a certain constitutional type or is it inherited, and, if so, are there any laws of heredity which it follows? How shall we answer this question when asked by a patient who is a descendent of a cancer family. Evidence for this by no means simple question comes from statistics on cancer, histories of families, study of twins, experimentation on animals, and the response of cancer strains to carcinogenic agents.

It was formerly taught that in lower animals at any rate carcinoma may be trans*mitted as a recessive character and will occur in the second generation in strict mendelian* ratio and that transmission may be through either sex but more commonly through the female. MacDowell states that dominance is only a special case at the end of a cutaneous series of interrelations between pairs of genes. No gene can produce its effect without cooperation of many other genes—and genes and extrinsic conditions cooperate in all cases. By inbreeding, involving brother to sister mating, many different strains of mice have been established with varying degrees of susceptibility to cancer. This genetic homogeneity shows among other characteristics that the inherited tendency or predisposition to develop cancer is not a general character but is confined to a *definite organ* or tissue type. Only in primary cancer of the lung (in mice) is the inheritance a hereditary dominant character although the dominance is incomplete. Tumors of different sites and types differ in their genetic behavior (see Chapter 10).

Some people are susceptible; that is, they react to stimuli (as yet not defined) with tumor formation. Others are refractory. In the former, factors exist which are inherited independently of a general disposition which govern the localization of the disease due to favorable local soil; such an individual with both general and local susceptibility is apt to get cancer. This is illustrated by studies in families with cancer in Holland and Norway. Patients with the disease, "basal patients," have brothers or sisters (siblings) or brothers, sisters, parents, aunts, and uncles with the disease much more commonly and at an earlier age than in "non basal" families; *this holds true for* a particular organ as well. Waaler has shown that in 100 women with cancer of the breast who had a sister with cancer, 45 would have cancer of the breast. Of 100 women with cancer elsewhere in the body with cancerous sisters, only 16 had cancer of the breast—*the general incidence. A study of 53 monozygous and 35 dizygous* twins was reported in which tumors occurred in one or both. The incidence in both members was greater in the former. The tumor was of the same type and occurred in the same organ and the age of onset was more nearly identical much more frequently in the monozygous than in the dizygous twin group.

Host Factors in Cancer.—A variable group of so-called host factors have been mentioned as contributing to susceptibility to cancer; among these are age, race, body weight, diet, and even social strata.

Age as an etiological factor is important, although only relatively so, because we now see cancer in much younger individuals than formerly. However, we may state that it is primarily a disease of those over, rather than under, 40 years of age. It is interesting to note in this connection that when carcinoma occurs in patients in the second and third decades of life, there is very rapid metastasis, whereas *in patients in* the seventh and eighth decades, there is a very slow one. The reverse is true of infec-

tion. *Thus, the older an individual, the less resistant the lymphatics to the spread of infection and the more resistant to the spread of neoplasms.* We do not know the cause of this difference. Since carcinoma occurs usually in the fifth and sixth decades, the difference in rate between the spread of infection and neoplasm is not apparent, because this is the middle ground. As we grow older there is an accumulation in certain older tissues of stimuli to growth and a sensitization as a result of these stimuli which are either hormonal or nonhormonal within the cell itself.

Fig. 116.—Malignant dermatosis. Clinical photograph of Bowen's disease of the skin or malignant dermatosis. (Carcinoma in situ of the skin.) Note the many areas of carcinomatous tissue, yet there are no metastases. Apparently all of these areas and progressing simultaneously. The patient had many operations, and the lesions were so numerous that it was deemed inadvisable to remove more than a few lesions at a time for fear of denuding too large an area of the skin.

The tissues of older and those of younger organisms seem to differ only quantitatively in their reactions as far as growth processes and cancerous processes are concerned. This quantitative difference is sufficient to make of cancer in the young a highly malignant, rapidly killing disease, whereas the same growth in the old *may* be so slow in its growth as to assume benign proportions. Cancer is slow to evolve. If it appears in the young there is a strong susceptibility and a powerful carcinogenic agent, a combination which makes the resulting cancer highly malignant. If the conditions are reversed,

cancer may not develop until a late age. *This accounts for the greater incidence in the older group.* Thus the longer the individual lives, the greater his chance of getting cancer. The mouse lives 2 years, the human being 70 years. Therefore, in speaking of 6 months of age in the former, we mean about 17 *years in the latter. If aging is a* process of disorganization and disintegration the disorganized cells producing cancer resemble not the old cells but rather youthful, even embryonic cells.

Different species of animals show various susceptibilities to cancer. Moreover, a greater variety of species is subject to the carcinogenic process than to any other disease. Spontaneous cancers have been found in insects, birds, reptiles, amphibia, fish, mice, rats, rabbits, dogs, cats, cattle, hogs, and sheep as well as in man.

Cancer of the skin is far more common in the white than in the colored race; there is nearly a total absence of gastric cancer in the native Malay population of Java, although the Chinese in Java have it; primary liver cell cancer is common in Java and Sumatra and in certain populations of Africa including the Bantus and the natives of Northern India, whereas it is uncommon in Europe and America. Japanese women have an extreme incidence of cancer of the uterine cervix (32 per cent) but a very low incidence of mammary cancer (3 per cent).

In both animals and man individuals of average or less than average weight are thought not as likely to develop cancer as those who are overweight; this is not unequivocally proved. *However, diet may play a role as a modifying factor in carcinogenesis.* The growth rate of spontaneous mammary carcinoma in mice is inhibited by diets deficient in certain essential amino acids (Voegtlin); hepatoma formation by butter yellow *has been observed; methylcholanthrene painted on the skin* of mice will produce acute leucemia if their diets have adequate amounts of cystine; on low cystine diets leucemia is greatly retarded and instead sclerotic lesions of the larger arteries are observed (Voegtlin).

The fact that cancer was found to be more prevalent in the lowest social class in England twenty years ago led to group studies of class incidence. Much of this data is now known to be the result of extrinsic occupational carcinogenic contacts. Cramer believes that "social cancer" is an experiment carried out by man on himself in his ignorance, and with increasing knowledge of the exogenous factors involved it should, like occupational cancer, become a preventable disease.

Carcinogenic Agents.—

Exogenous Causes.—The number of provocative carcinogens is so great that many can only be mentioned here. Indeed carcinogenicity is influenced by such factors as species, genetic constitution, age, sex, diet, physical condition of the animal, purity of the chemical compound, dose, physical state of the compound, nature of the solvent or vehicle used, and site of application. If, however, there is an inciting agent for every spontaneous tumor, we must attempt to find it. Some of the agents are already known. Substances which produce cancer in any animal are known as pancarcinogens; some examples are certain of the polycyclic hydrocarbons (methylcholanthrene, benzpyrene), x ray, gamma ray of radium. *Provocative carcinogens bring about changes in tissues* which may or may not cause tumors. Most carcinogenic agents belong in this group. Rous calls the viruses actuating carcinogens. Some agents excite specific tissues to tumor formation: betanaphythylamine affects urinary bladder epithelium; estrone in experimental animals affects breast and uterus.

Occupational inciters include chemical and physical agents such as arsenic, chromates, nickel, carbonyl, radium, mesothorium, asbestos, crude mineral oil, pitch, tar, soot, paraffin oil, anthracene oil, creosote, aromatic amino compounds such as *aniline*, nephthylamine and benzidine, benzol, ultraviolet rays, roentgen rays, rays of radioactive substances including the atomic bomb, certain parasitic worms.

Habits and environmental stress may be responsible for cancer of the mouth, lips, and cheeks in tobacco smokers, betel nut chewers in Siam, fishermen holding tarry needles in their mouth in repairing nets, for cancer of the skin of the abdominal wall in

carriers of certain heating appliances in Kashmir or in Japan—kangri cancer, mule spinners cancer in England, exposure to the sun and wind in "outside" workers.

Trauma has usually been considered as a primary cause of cancer by patients as well as by physicians. Women with cancer of the breast usually recall an injury to the affected breast. "Chronic irritation" while still invoked for cancer control education lacks scientific confirmation experimentally or clinically. One often wonders why the little toe which is irritated by ill-fitting shoes to such degrees that *corns, calluses,* and deformities result is almost never the site of carcinoma. *Single* trauma as an etiologic factor in carcinoma is difficult to prove. At present this question has great medicolegal interest. Our own feeling is that if a single injury is the cause, then such an injury when induced by incomplete surgical removal of a benign neoplasm should

Fig 117.—Bowen's disease of skin (malignant dermatosis). Medium-power photomicrograph of skin in Bowen's disease. *A.* Hyperkeratotic epithelium and leucocytes forming a scab over the lesion. *B.* Malignant acanthotic germinal layer. *C.* A papilla of the dermis showing increased vascularity and many inflammatory cells. *D.* Enlarged rete peg showing irregularity of cell structure. It will be noted that there is no breaking through of the malignant area into the underlying tissue. (Squamous-cell carcinoma in situ)

result in a malignant growth. Marjolin called attention to the fact that not infrequently carcinoma arises in the chronic ulcer following a burn in the lower extremity. This may be cited as a single trauma supplemented by chronic irritation. The incomplete removal of melanomas composed of pluripotential chromatophore cells is followed by malignant melanoma often enough to make one wonder whether or not here is an exception to the fairly accurate observation that single trauma is not often the cause of cancer.

Infections may be cancer inciters as discussed under the heading of Endogenous Causes. An old observation which is fairly accurate is the infrequency of cancer in

cancer may not develop until a late age. This accounts for the greater incidence in the older group. Thus the longer the individual lives, the greater his chance of getting cancer. The mouse lives 2 years, the human being 70 years. Therefore, in speaking of 6 months of age in the former, we *mean about 17 years in the latter. If aging is a* process of disorganization and disintegration the disorganized cells producing cancer resemble not the old cells but rather youthful, even embryonic cells.

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Habits and environmental stress may be responsible for cancer of the mouth, lips, and cheeks in *tobacco smokers, betel nut chewers in Siam, fishermen* holding tarry needles in their mouth in repairing nets, for cancer of the skin of the abdominal wall in

augmented by a virus. When such a growth is pent up under the foreskin aided by inflammation and maceration, it may become malignant.

Animals may develop an immunity to viruses. Rabbits in which carcinoma is transplanted become strongly immune to the virus as the growths enlarge. Viruses require only slight tissue preparation (trauma of susceptible tissue with the virus) and therefore cannot be the cause of tumors generally. *There is no proof today that any human malignant tumor is induced by a virus.* Attempts to cause cancer with tumor tissues or tissue juices from man has failed and there is no record of a nurse's or a physician's acquiring sarcoma or carcinoma by contact unless the incubation period is a matter of years. Crude tissue extracts reported to have carcinogenic qualities are all associated with lipids or fats—in animals, extracts from tumors, liver, bile, urine, and lungs have produced tumors.

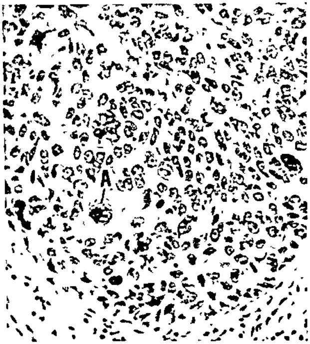

Fig. 118.—Bowen's disease of skin (malignant dermatosis). High-power photomicrograph of a rete peg shown in the previous illustration Note the nuclear agglutination and irregularity in size and shape of the nuclei. Note that the cells have been retained within the rete peg and have not infiltrated into the underlying tissue.

A, Large and multiple nuclei of a neoplastic, squamous epithelial cell. Bowen's disease. illustrates a type of squamous-cell carcinoma which is multicentric, which does not metastasize until very late. The reasons advanced for its peculiar behavior have been that there is very much tissue reaction about the new growth (round-cell infiltration and fibroplasia) so that it does not reach the lymphatics and is, therefore, not disseminated by them.

Carcinogenic agents from human sources include cholesterol and other sterols, the sex hormones, D vitamins, bile acids, myelin, and others. They have been mentioned under exogenous causes. However, when such compounds are present in excessively large amounts in the body, they may become endogenous carcinogens. The action of sex hormones in this capacity may arise from the following: (1) By stimulating gland tissue to develop they provide the cells on which other carcinogenic agents may act. (2) If supplied in excess they may themselves produce the tissue disorder out of which tumors come. (3) They may urge neoplastic cells on so that they multiply into tumors as in prostatic cancers which regress after orchiectomy. (4) They may act in combinations of the foregoing.

patients who have had a severe infection such as typhoid fever, scarlet fever, or other streptococcic septicemias. The use of Coley's mixed toxins (Bacillus prodigiosus and *Streptococcus erysipelatis*) in the treatment of sarcoma is based on this concept or on the phenomenon of Arthus and Shwartzman. A very interesting disease supposedly viral in origin occurring in South African sheep gives rise to a pulmonary adenomatosis known as Jagziekte. It is contagious among sheep and is known among sheep herders as "snotty nose." The important facts about this disease are that it occurs in man and is probably a multicentric malignant tumor of epithelial origin in the alveoli of the lung—an alveolar-cell carcinoma. Metatases are almost unknown. In this regard it resembles multiple malignant polypi of the colon or multiple squamous-cell carcinomas of the skin. The disease Jagziekte is contagious in sheep and the incubation period is relatively long. Is this disease and other forms of lung cancer contagious in man and not recognizeable as such because of the very long incubation period which extends over years rather than days or weeks?

Stimulation of certain tissues by trauma as well as by hormones will induce growth—not necessarily neoplasia. An organ or tissue increases in size by (1) increased blood supply, (2) increase in tissue fluids, (3) enlargement of cells (hypertrophy) and increase in numbers of cells (hyperplasia). Swabbing the vagina in mice stimulates growth of cells and new cells from two to more than twelve layers in forty eight hours. The chronic disturbance on which carcinoma arises is not known.

Exogenous agents may affect cells grown outside the body. Rat and mouse fibroblasts grown outside the body in a medium containing methylcholanthrene are changed into cells which resemble cells in cultures of sarcoma induced by this substance when injected into the subcutaneous tissue of rats. The transformation is irreversible. In turn the fibroblasts subjected to this action can produce sarcoma when injected into mice, even if done months after exposure, thereby eliminating a carry-over of the chemical. This same substance may induce mammary cancer.

Normal cells and their descendants can be made cancerous in vivo and in vitro but they cannot be made normal again. Once cancer is produced or occurs it cannot be reversed or stopped unless destroyed or removed.

Endogenous Causes.—Viruses may be exogenous or endogenous, but one type is definitely from sarcoma. Peyton Rous has produced chicken sarcoma by transplanting a substance thought to be a filtrable virus. Perhaps some of the tissue juice is the provocative agent. Rous contends that the only carcinogenic agents which are known to produce tumors by direct action are the neoplastic viruses. Agents which call forth carcinoma and sarcoma evoke a wide variety of neoplasms—from the most malignant to some which have so little initiative that they need help to survive. Therefore, the benign tumor and the cancer are only individual expressions of a single neoplastic principle. Deviations from this principle, as Kaposi's sarcoma (xeroderma pigmentosum), are rare. Normal cells while functioning may behave for a brief while as if neoplastic—the chorion, for example. The agents which call forth tumors in experimental animals are probably not the actuating causes of the growths they call forth. Many of them may be gone months or years before tumors develop. Animal parasites causing growths such as tubercle bacilli, Bilharzia, cysticercus (sarcoma from cyst wall in rat livers) are left behind as the tumors, which they may have started, enlarge. The irreversible intracellular change, once it has occurred, persists within the cell even after the carcinogenic agent has been removed or eradicated. Thus the autonomous infiltrative growth of the cancer cell is a property residing in the cell. Rous believes that viruses render normal cells neoplastic when injected in experimental animals and they maintain a partnership with them. All were originally gotten from spontaneous tumors and they give rise to growths like those from which they came. They are specific and act only on closely related species. Sometimes they may be provocative instead of actuating as in condyloma accuminata which we have seen is the result of irritation perhaps

cancer. The body resists excess of estrogen by detoxification; a part of this task is done by the liver. It is difficult to see how estrogenic hormones given in therapeutic doses to normal women could act as carcinogens. There are exceptions to this statement, such as bleeding from the nipple, metrorrhagia, etc., which will be discussed in other chapters. Recently a case of cancer of the endometrium was reported due to prolonged estrogen therapy without adequate rest periods.

Transplantation of Tumors.—We have seen that attempts to cause cancer with tumor tissue from man have failed. This does not mean that carcinoma cannot be transplanted from one portion of the body to another in individuals with this growth. Following the Mikulicz operation for carcinoma of the colon, cancer cells may be transplanted into the skin. Excessive handling of malignant tissue by the surgeon may actually transplant these cells. Recently a case was reported of transplantation from cancer of the breast to the donor site for skin graft on the opposite thigh which was taken at the time of radical mastectomy. Heterogeneous transplants have recently been done in animals by Greene and Saxon. These transplants survived and grew but they are essentially grafts which exist as parasites in the new host. They are not new tumors composed of cells derived from the host under the influence of a cancerigenic *agent carried by the tissue. The fact that tumors can be transplanted in series* in experimental animals demonstrates that malignancy is centered in the cells, since the new tumors resulting from the transplanted old ones are formed entirely by the multiplication of the introduced cells. But in spite of the intimate contact between the host's tissues and the tissue of the tumor for which it supplies blood vessels and supporting stroma, this does not lead to a malignant character change in the host's cells. In other words, the transplant is a graft and is limited by the same biological laws as those governing normal tissue grafting. Previously we spoke of natural resistance to cancer. This is not a resistance against cancer as a disease, as is the natural or acquired immunity againt tuberculosis or other diseases. It is the resistance against introduced cells of another individual of a different genetic make-up. In man this is evident in attempts at heterogenous, homogenous, or even isogenous skin grafts, even though whole organs such as a section of aorta have been successfully transplanted from man to man.

Transformation of Normal Cells Into Cancer Cells.—The transformation of normal cells into cancer cells lies within the cell partly at least in the cytoplasm, and the change is permanent and irreversible, making it possible for the cell to keep proliferating without any stimulus. This new property is a fixed character of the cell and is transmitted to all its descendants. Neoplastic change is not a mere exaggeration of chronic inflammation which it does resemble at the beginning. It is new, abnormal, and abrupt and is irreversible. Furthermore, it may not take place everywhere throughout normal tissue but here and there. When tumors appear on the basis of developmental anomalies they are said to be carcinogenic in that they provide a terrain suited to neoplastic change (von Recklinghausen's disease, intestinal polyposis).

In colon carcinoma a potentially malignant region exists prior to or coinci*dentally with the development of cancer. It is larger than the cancer itself* and its cause is unknown. There is an inflammatory reaction and the cells primarily concerned are mesoblastic which are the natural defense cells of the body. The effect on the epithelial cells is secondary and represents a stage of partial destruction or impairment of nutrition followed by a stage of attempted repair. The repair goes wrong (1) if a portion of the epithelium is isolated from the rest of the layer by a ring of lymphoid tissue as in polyp formation or (2) if epithelial cells become displaced into deeper parts of the submucous tissue as after ulceration.

Restraining Influence.—The factors governing the onset of malignancy seem to be not in the epithelial cells but in the mesenchymal cell system. Subepithelial connective tissue reacts with hyperemia and cells (leucocytes) followed by fibrosis, and this precedes

Cancer of the breast in mice involves three endogenous factors: (1) the genetic constitution or the hereditary susceptibility, (2) the presence of the female hormone estrone, and (3) the presence of the so-called mammary tumor inciter or "milk-factor." The latter is said to be present only in strains with a high incidence of spontaneous mammary cancer; it is absent in strains with a low incidence. Mice from a high cancer strain fostered by females from a low cancer strain have a lower breast cancer rate than litter mates nursed by their own mothers. The reverse is also true; that is, young from a low cancer strain fostered by females from a high strain have a higher mammary cancer rate. The tendency toward cancer of the breast is transmitted in greater intensity by the female than by the male; and factor (2), the presence of the estrogens as a cancer-producing agent, manifests itself more clearly in those strains with a high natural tendency; if the ovaries are removed at early sexual maturity, the rate drops almost to zero.

Since estrogens are partially detoxified in the liver and since thiamine is necessary for efficient liver function, low thiamine-high estrogen levels have been studied in uterine cancers. This combination is thought to be related to the cause of the disease.

Estrogenic hormones produce growth in the female genital organs. In normal animals after a brief period of activity there is retrogression, especially in the vagina and uterus and to some extent in the mammary glands. When the hormone is given in large doses continuously the genital organs do not regress and rest briefly after short phases of growth and function. Under such conditions it is possible to produce abnormal growths, atypical growths, and, in some cases, cancer. In monkeys a different effect may result; the uterus atrophies and the breasts keep growing. In cancer mice sexual cycles finally disappear and the vagina and uterus become atrophic and the ovaries small. If estrogens are injected, full growth of these organs returns, although the estrogens do not seem to affect the growth of the cancerous nodules. In male mice or low strain female mice (less than 5 per cent) large doses of estrogen may be carcinogenic.

Endocrine imbalance may cause spontaneous tumors; for instance, the secretion of estrogens by testicular tumors. The same condition has been found in dogs and also in mice; tumors or hypertrophy of the pituitary, ovaries, uterus, and mammary gland may affect each other. In mice transplanting the testes in females makes the pituitary enlarge which in turn stimulates the ovaries to produce a large quantity of hormone. Such mice develop cancer. This experiment refutes the charge that the dose and amount of hormone used experimentally in the production of cancer cannot be equaled by the animals' own production. However, this does not take into account the effect of antihormones or neutralizing factors which may be present in the body.

Estrogens affect tissues not primarily reproductive such as enlargement of the birth canal in certain animals, formation of new bone in marrow cavities, greatly increased phosphorus and calcium levels in birds. All effects can be reversed by the injection of male sex hormone. Testes will atrophy if estrogens are long continued in male mice.

Fibromyomas occur in guinea pigs after estrogen stimulation and not carcinoma—this is comparable to the rarity of carcinoma of the uterus in colored women and the prevalence of fibromyoma.

No cases of spontaneous cancer of the uterine cervix have been reported in mice—a few have occurred after estrogenic stimulation but the mice developed mammary cancer first—the genetic and tissue susceptibility are different. The mammary glands are most responsive to estrogens, then the epithelium of the vagina and cervix, and lastly the uterus and adnexa.

The highest incidence of carcinoma in the human female genital tract occurs at or after the menopause. Ovulation usually ceases after the menopause. This eliminates corpus luteum from periodically modifying or interrupting estrogenic stimulation which may still be present, resulting in an endocrine imbalance which may be conducive to

If any conclusion can be drawn from this review concerning the causes of cancer, it would be that progress is being made by clinical and experimental researchers. Our treatment at present is empirical because we have not broken down the barrier of causation. Cancer is probably a group of diseases very much like infections which represent a group of diseases, all evoking more or less similar tissue changes yet each one different, depending on various etiological agents. Moreover, one agent may produce more than one kind of cancer just as one type of microorganism may evoke various responses. It is, as in infections, probably the "potency" of the carcinogenic agent, the "ferocity" with which it acts, and the "defense" which the body is able to bring into play that determines the type and malignancy of the disease.

Nomenclature and Classification

The best way to classify tumors would be as we did with ulcers (see Chapter 6)—on an etiological basis. Obviously this cannot be done since in only a few instances is this possible with our present knowledge of the cause of new growths. The classification in the text is modified from Ewing and is based on the *histological* appearance. A histogenic classification would be better but this is not always possible. Such terms as neurofibroma, as distinguished from perineural fibroblastoma, is an attempt to show origin. When structure varies, histogenesis dominates the name—adamantinoma, hypernephroma, etc. We have used the word *blastoma* which means a true neoplasm of independent growth, usually of one embryonic layer and a predominance of adult cells. The word is derived from blastomere in which the cells are undifferentiated and hence blastoma is not a fully justified term used in its present connotation. Since adult tissues have various embryological derivations, we cannot classify according to germ layers such as ectodermal, entodermal, and mesodermal. Adami points out that there are two main tissues from early embryological processes which permanently retain their early characters; namely, lining membrane tissues, which he calls lepidic, meaning membrane, and pulp tissues or hylic, meaning crude matter. The former are composed of specific cells not penetrated by blood vessels and possess no stroma. The epiblast and hypoblast are primary and the mesothelium and endothelium secondary lepidic tissues. Hylic or pulp tissues are composed of cells separated by a homogeneous fibrillar stroma which may or may not be penetrated by blood vessels; the mesenchyme is of this type. Although oncology is not a part of embryology and anaplasia has little in common with the latter, yet it is of help in interpreting tumor growth, especially teratomas, and therefore the terms suggested by Adami are included in this classification.

The suffix *oma* means swelling; to indicate a particular growth it is preceded with the name of the tissue which makes up its main cellular structure. Tumors like normal tissue have various components. There is always the trunk and branches (blood vessels and connective tissue) and the leaves of flowers (epithelial elements) to every tree. So it is with tissue or organs. In a papilloma the significant component is the epithelial tissue

any alteration in epithelial cells. This resistance which checks the development of the initial malignant growth has been termed "primary resistance." While the cancer increases by autoplasty and spreads by metastasis, the rest of the area where malignancy may occur, which may be large, is not invaded by further or multicentric newgrowth due to "secondary resistance" caused by the presence of the initial cancer. If, however, the primary cancer is removed, then secondary cancer may be produced although it could not be induced as long as the primary growth was there. It may take six months in mice to get the secondary cancer to grow. This is equal to sixteen years in man. Is the removal of a cancer in man a check to autoplasty only? Then after the "secondary resistance" has ceased to act may a new cancer develop due to causes which *precipitated the first growth; that is, a second primary carcinoma?* This interesting speculation may explain five- or ten-year cures but the rarity of fifteen-year cures.

The restraining influence in cancer is, first, that of any foreign group of cells—an inflammatory reaction which tends to remove or destroy the invader and to localize such elements as cannot be eradicated. This is not a new phenomenon, for we have studied it in all types of injuries. It is clearly illustrated in the difference between *squamous-cell carcinoma and a special variety of malignant dermatosis or Bowen's disease.*

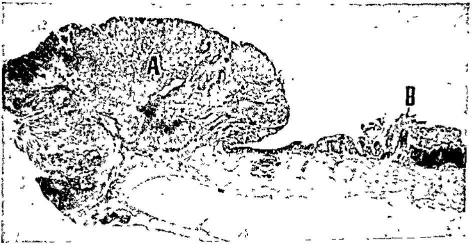

Fig 119.—Infiltrating carcinoma in Bowen's disease (low-power photomicrograph). Infiltrating carcinoma developing in an area of malignant dermatosis. *A.* Carcinoma arising in Bowen's disease which has penetrated into the underlying tissue. *B.* An adjacent area without penetration. Note the invasion of the stratum papillare of the skin in *A.*

Precancerous Conditions in Man.—With the advent of experimental cancer it became evident that even after a carcinogenic agent was applied much time elapsed before cancer resulted. During this time the tissue undergoes a pathological change which is not always apparent. In man most precancerous lesions have been noted on the skin (see Chapter 16). However, precancerous lesions have been noted elsewhere as in syphilis of the tongue, leucoplakia of the mouth, kraurosis vulvae. The precancerous conditions are not necessarily hyperplasia as in experimental skin cancer but may be epithelial atrophy. Atrophic lesions are radiation dermatitis, atrophic undescended testes, kraurosis vulvae, gastric ulcer, and chronic atrophic gastritis, although in the latter instance we are not sure whether it is cause or effect. Hyperplasia is more commonly a precursor as seen in gastric polyp, congenital polyposis of the colon, etc. More will be said of "precancerous lesions" in subsequent chapters. The term is equivocal because not in all cases are we sure of the forerunner of cancer and no sharp line of demarcation can be drawn between the precancerous and cancerous process. Perhaps precancerous lesions are carcinoma in situ if we could only find the cells.

even though there is a stalk with blood vessels and connective tissue; hence it is an epithelial neoplasm. Complex names such as fibroadenoma and fibromyoma are used to describe growths which are composed of more than one type of tissue. The prefix denotes the tissue which is present *in less amount: thus a fibroadenoma is an adenoma with some fibrous* tissue. They are simple mixed tumors. New growths with tissues or organs of one or all the embryonic layers are known as teratomas and are found usually in the ovary or testis. The plural of *-oma* is *-omas* or *-omata.*

Some terms which have been used for almost ninety years are probably not accurate. Myxoma is not a special type of new growth as listed below but is probably a connective tissue neoplasm which holds interstitial mucus. "Colloid" carcinoma is wrong because the substance is probably mucus and should be called mucous carcinoma. Other tumors which have recently been questioned are the adenomas which are thought by some to be hyperplasias and not true tumors and hemangiomas which in many instances are congenital anomalies, not neoplasms. Lastly, the term benign or innocent is always open to question. When is a true tumor innocent? Knowing the limitations of nomenclature permits us to set forth various terms which are currently used even though some are of historic interest only.

Classification (Histogenetic)

I. Epithelial neoplasms (lepidic)
- A. Benign
  1. Papilloma—a benign tumor of pavement epithelium with supporting tissue in normal arrangement
  2. Adenoma—a benign tumor of glandular epithelium with supporting tissue in normal arrangement
- B. Malignant

  Carcinoma (*carcinos*, crablike)

  Carcinomas may be further classified as follows:
  1. Consistency
     - a. Encephaloid or medullary—soft
     - b. Scirrhus—hard
  2. Type of epithelium
     - a. Simple epithelium
       - (1) Columner (in intestines, etc.)
       - (2) Cuboidal (in breast, etc.)
       - (3) Squamous (ear, Bowman's capsule, rete testes, and smallest excretory ducts of many glands)
       - (4) Transitional
     - b. Stratified epithelium
       - (1) *Squamous cell*
       - (2) Basal cell
       - (3) Combined
  3. Architecture
     - a. Adenocarcinoma, resembling glands
     - b. Carcinoma simplex, with a solid palisade of cells

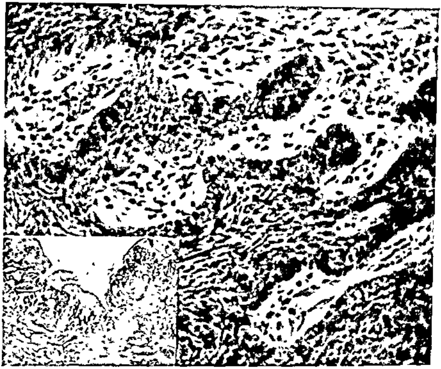

Fig. 120.—Basal-cell carcinoma (rodent ulcer) of the neck. The low power shows the ulcer and invasion of subcutaneous tissue The high power shows malignant cells, which originate from the *stratum germinativum* (Malpighian layer).

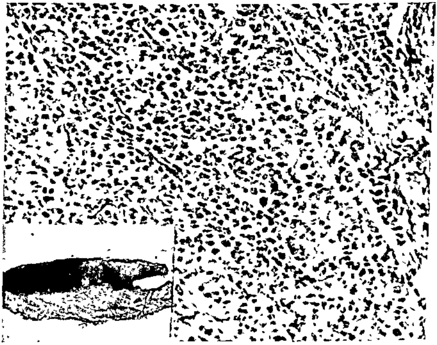

Fig. 121.—Malignant melanoma (from the arm). The low power shows the invasiveness of the tumor; the high power shows the lepidic arrangement of the cells. This has led to difference of opinion in classification, some naming the lesion melanosarcoma, others, melanocarcinoma. *The malignant cells are atypical in size, shape, and staining reaction.*

3. Nervous system (mesenchymal and epithelial parts)
    a. Glioma or neuroglioma—composed of neuroglia astrocytes, oligodendrocytes which are ectodermal and microglia which is mesodermal
    b. Neuroepithelioma—from neuro-epithelium
    c. Neuroma—nerve fibers and cells
    d. Neurolemmoma—Schwannoma or perineural fibroblastoma—neurolemma
4. Endothelioma—endothelium
    a. Angioendothelioma

B. Malignant
1. Sarcoma (*sarcos,* "meatlike"); are malignant tumors of connective tissue origin with cells and supporting tissue abnormal in morphology and arrangement
2. Immature forms—undifferentiated cells
3. Mature forms—more like normal cells
    a. Spindle cell sarcoma
    b. Round cell sarcoma
    c. Fibrosarcoma
    d. Chondrosarcoma, etc.

III. Mixed neoplasms

A. Simple mixed tumors—made up of more than one type of tumor tissue—benign-like fibroadenoma, malignant-like chondroepithelioma; adenosarcoma

B. Teratoma—monodermal, bidermal, or tridermal—tissues and organs of one, two, or three germinal layers

C. Embryoma—composed of tissues from three germinal layers in more or less orderly imitation of a fetus

D. Malignant
1. Sarcoma
2. Carcinoma
3. Sarcoma-carcinoides

General Observations Concerning New Growths

Incidence of Cancer.—Approximately 200,000 persons are expected to die of cancer in 1950. There are now between 600,000 and 1,000,000 people in the United States who know they have cancer. One of every 5 to 6 persons who die between the age of 45 and 70 years die of cancer. More people are living beyond 40—at present, 30 per cent. By 1980, 40 per cent of our population will be over 45 years of age—the cancer age group.

Cancer mortality by organ primarily affected as given by the 1942 United States Census showed 163,400 *cancer deaths. Table XII* shows a comparison between the figures of the United States Census Bureau in 1942 and figures from The National Cancer Conference in 1949.

This may not be entirely accurate because often the primary site is unknown—the metastatic area may be the only detectable region or organ involved.

1. A metastatic growth may overshadow the original if its environment is favorable. Example: Carcinoma of the sigmoid colon may grow slowly for years and then may metastasize to the liver and grow rapidly in this organ.

c. Carcinoma "in situ"—malignant cells have not as yet broken through surrounding tissues out of their parent epithelium

4. Function

Mucoid; since the epithelium functions in a rudimentary way, mucus may appear or there may be colloid degeneration; also called colloid, gelatinosum, or collonema.

5. According to histogenesis

a. Neuroepithelioma, composed of neuroepithelium

b. Choriocarcinoma, from chorionic epithelium

6. Reaction of tissues

Inflammatory carcinoma—vigorous tissue reaction with rapid spread

II. Mesenchymal and mesodermal (hylic) neoplasms

A. Benign

1. Connective tissue; are benign tumors of connective tissue origin, with supporting tissue in normal arrangement

a. Fibroma—fibrous connective tissue

b. Chondroma—cartilage

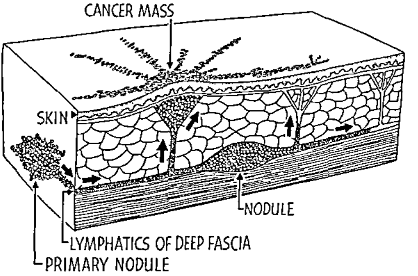

Fig. 122.—Diagram illustrating Handley's theory of permeation in carcinoma. The primary carcinoma is shown on the left. Cancer cells permeate along the tubular lymphatics on the deep fascia and then grow up the communicating vessels to the reticular lymphatics of the skin. A secondary nodule is indicated on the deep fascia, and the cancer mass seen in the skin is shown to have permeated also in all directions. A reaction takes place in the lymphatics (perilymphatic fibrosis), which results in their occlusion after the cells have permeated the area. In cancer of the breast this occlusion gives rise to edema (pigskin appearance *early*, and cancer en cuirasse *late*). Permeation is more rapid in the deep than in the superficial lymphatics; therefore, more fascia than skin should be removed. However, a wide area of skin is also involved, as shown.

c. Chordoma—chorda dorsalis (nucleus pulposus)

d. Osteoma—bone

e. Myxoma—mucous tissue (like Wharton's jelly)

f. Lipoma—fat tissue

g. Angioma—vessels

h. Hemangioma—blood vessels

i. Lymphangioma—lymph vessels

j. Lymphoma—lympoid tissue

2. Muscle tissue

a. Leiomyoma (smooth muscle)—mesenchymal

b. Rhabdomyoma (striped muscle)—mesodermal

prostate). *A third group include those organs not often affected by* primary or secondary growths (spleen, heart, skeletal muscle).

4. Tissue cells may be kept growing and reproducing for years in an artificial medium but they lose their power to differentiate into a particular kind of cell, such as epithelial, endothelial, muscle, etc. If connective tissue cells are added, they differentiate. *Cells devoting their whole energy to reproduction can do nothing else.* This may explain the dedifferentiation of rapidly growing, highly malignant neoplasms. Conversely, cells which exhibit a function (produce secretions, mucus excretions, bone) resembling their original duty are apt to be less malignant.

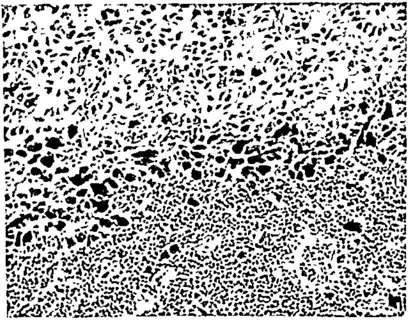

FIG. 123.—Lymph node showing metastatic melanoma. The growth metastasizes by the lymphatics (the nodes becoming dark in color) and by the blood stream (high power).

5. Certain cells may be inherited (in some people) which do not keep step with normal growth when a certain time in life is reached—instead, they grow wildly. This "certain time" may be hastened by deliberate exposure to carcinogens, exogenous and/or endogenous, and neglect of ulcerations or other precancerous changes.

6. Resistance: "The presence of large numbers of lymphocytes about the inoculated tumor and also about human malignant tumors makes it seem probable that these cells offer some special resistance to tumor growth." (MacCarty and Kehrer.)

We have seen that malignant tumors are known to have regressed and that the incidence of such growths is less in persons who have had severe infections such as erysipelas, peritonitis accompanied by high fever, and toxemia. It is now thought that this protection against tumors is due mainly to local tissue reactions. Illustrations of the efficient pro-

TABLE XII

	UNITED STATES CENSUS, 1942 (%)	NATIONAL CANCER CONFERENCE, 1949	
		MALE (%)	FEMALE (%)
Digestive organs and peritoneum	45.7	49.7	
Stomach	16.1	18	10.3
Large and small intestines	11.5	11.2	12.8
Bile tract and liver	6.3	5.4	6.4
Rectum and anus	5.4	6.4	4.6
Pancreas	3.5	4.4	3.2
Esophagus	1.7	3.0	0.7
Mouth and pharynx	3.2	4.8	1.2
Other sites	1.2		
Uterus	10.0		18.5
Cervix	8.0		
Body	2.0		
Breast	9.2	1	18.5
Respiratory system	6.2	13.5	3.5
Lung	4.0	7.4	2.5
Larynx	1.0	1.8	0.2
Bronchus		3.7	0.6
Other sites	1.2		
Male genitals	5.9	13	
Prostate	5.4	12	
Other sites	0.4	1	
Urinary tract	4.7	6.3	3.4
Bladder	3.1	4.2	2.1
Kidney	1.5	2.0	1.2
Buccal cavity and pharynx	3.2	4.8	1.2
Pharynx	1.0	1.6	0.4
Tongue	0.7	1.2	0.3
Other sites	1.5	1.0	0.5
Ovary, tubes, vagina, etc.	2.2		5.8
Skin (except vulva, scrotum, and lip)	2.0	2.4	1.5
Brain and cord	1.6	2.1	1.4
Miscellaneous or unspecified	7.6	6.9	5.7

An example is the fact that metastasis, in primary melanotic sarcoma of the eye, is most frequent and attains greatest growth in the liver. This would seem to indicate that the liver tissues offer favorable conditions for the growth of this particular tumor. The frequency of the involvement of the liver in secondary tumor originating in the stomach is easily explained by anatomical relationship. Conversely, the spleen is an organ which rarely shows invasion by carcinoma. The spleen also frequently escapes even when there is widespread dissemination of sarcoma. This organ is richly vascularized and should be open to invasion by tumor cells floating in the blood stream. The spleen is frequently the seat of infarction, and it can therefore be assumed that foreign material floating in the blood stream is likely to be deposited there. Unless tumor emboli follow different physical laws of circulation and deposition than do other emboli, it would seem the spleen itself offers some *resistance* to the tumor growth. This may be due to the rich content of lymphoid cells in the spleen, since the studies of Murphy indicate that lymphocytes protect against tumor growth (Karsner).

2. The older organs in the phylogenetic scale are more resistant to carcinoma (small intestine, muscle), the younger less resistant (stomach, breast, rectum, uterus).

3. An organ not usually the seat of primary malignancy is often the site of metastasis (for example, the liver, bone marrow, lymph nodes). The reverse is also true; that is, organs commonly the seat of primary tumors are rarely the seat of metastasis (stomach, breast, pancreas,

action of estrogen. After pregnancy estrogen can act unopposed because progesterone is considerably diminished.

Our conclusions are as follows: (1) There is no proof that pregnancy starts a "latent" carcinoma into activity. (2) If carcinoma is present, the growth keeps pace with the proliferation of new cells (hyperplasia) and enlargement of old (hypertrophy). The environmental tissues and stimulated breasts are growing in size rapidly and

FIG 125.—Metastases to the tibia. Same case as shown in Fig. 124.

their resistance is high due to increased blood supply. The intrusion of malignant cells is resented and opposed by inflammatory changes—inflammatory carcinoma. (3) The trauma of birth and necessary repair may be a stimulus to cancer. (4) Involutional changes and transplantation of epithelial elements post partum may increase the rate of growth.

As a result of these concepts in carcinoma of cervix, (1) we have urged careful inspection of breasts and cervix during pregnancy and es-

tection against tumors by local tissue reactions are (1) local "immunity" conferred by light x-ray therapy against implantation of *experimental* cancer; (2) cure of certain cancers by local application of arsenic and other chemicals; although such diversified agents as potassium, arsenite, glycerine, Coley's fluid, carcinomatous glands, and solution of leucocytes may destroy malignant (not normal) cells, yet they all set up an inflammatory response which may be responsible for tumor regression; (3) transplanted mouse tumors may be cured by starch injection through *lymphocytic and different natural defense reaction in resistant animals;* (4) spontaneous recession or cure of malignant growths in patients by severe infection or inflammation; (5) partial or complete breakdown of tumors following the asphyxia produced by ligation.

Fig. 124.—Metastasis from malignant melanoma to the hypothalamic area of the brain. The original lesion was in the skin posterior to the ear. Arrow points to pigmented tumor mass.

Immunity cannot readily be induced in splenectomized animals and Murphy has found that the chick embryo will not resist implantation of tumors until the spleen and lymphocytes have appeared. Murphy *and* collaborators reduced the lymphoid tissue and the circulating lymphocytes *by employing the x-ray and found that there* was then a decreased resistance to tumor implantation. When they increased the number of lymphocytes in mice by the use of dry heat, they demonstrated a high degree of immunity to certain transplantable tumors.

7. Carcinoma and pregnancy: Carcinoma does not often occur during pregnancy *(1 to 2,476 labors—Danforth) probably* due to the fact that the disease is seen in an age usually past the reproductive period. We have seen it in the cervix and breast and have studied it carefully. Many observers state that carcinoma grows faster and metastasizes earlier in pregnancy. Others hold that cancer is slowed due to the fact that corpus luteum *hormone (progesterone)* checks the blastomogenic

Such symptoms and signs as *great loss of weight, anemia, generalized metastases,* the presence of a large ulcerative growth, severe pain, and cachexia occur in the *late stages* of malignant growths. Cachexia may be due to many factors, such as hemorrhage, interference with important functions (digestion, excretion, respiration, deglutition, etc.), secondary infection, and the absorption of toxic products from degenerated tissues. All may play a role in producing this ghastly picture.

The second method of diagnosis is by *x-ray* and the use of *endoscopy* (proctoscopy, cystoscopy, bronchoscopy, esophagoscopy, gastroscopy, etc.).

Fig. 127.—Primary bronchiogenic carcinoma of the lung. Note the extension of the growth beyond the bifurcation of the bronchus. The patient was a man aged 64 years who complained of chronic cough. A large metastatic nodule in the liver was palpable.

The third, and perhaps most important, method of diagnosis is *biopsy,* with careful study of the excised tissue under the microscope. Biopsy is not dangerous if properly done. This has been studied experimentally and clinically. In rats biopsies of transplanted adenocarcinoma does not affect the average survival period of the animals or increase the percentage with lymph node and lung metastasis. In man many writers have claimed that cautery biopsy actually forces cells into lymphatics, that instruments used in taking biopsy may transplant cells, in sarcoma malignant thrombi may break loose and be carried to the lungs in a

pecially if there is bleeding from the nipple or vagina. (2) In the early stages of pregnancy if cancer is proved and the patient willing, the pregnancy is disregarded and surgical and radiotherapy is used. (3) In the late stage of pregnancy—cesarean section with supravaginal hysterectomy and bilateral oophorectomy is performed, followed by radium and x-ray treatment to the cervix. In the breast we have done a radical mastectomy at once and followed it with x-ray therapy. In early pregnancy we have tried both hysterectomy with bilateral oophorectomy and x-ray which causes an abortion and stops ovarian function. The results were discouraging. In late pregnancy we have allowed the patient to go to term. Carcinoma and pregnancy is a highly malignant combination.

Fig. 126.—Adenocarcinoma of the stomach.

Diagnosis of New Growth

The diagnosis of a new growth depends first upon the *clinical manifestations.* These will be discussed in succeeding chapters under the systems in which they occur. Three clinical signs must be kept in mind in relation to cancer: (1) a lump or swelling in an organ; (2) a sore which does not heal readily; (3) an abnormal or bloody discharge or secretion from a gland or viscus. The following symptoms are equally important in connection with the foregoing signs: (1) absence of pain (in early stages) and (2) disturbance of function (indigestion in gastric carcinoma; constipation, or diarrhea, or alternation of these in carcinoma of the colon), overproduction of a hormone (pancreas) or production when normal function is over (theca-cell tumor of ovary), or perverted secretin (arrhenoblastoma), etc.

then staining or the material may be spread on a slide. The technique in general is fixation with equal parts of 95 per cent alcohol and ether and staining with hematoxylin and the O G 6 and E A 36 stains. (Papanicolaou.) See Chapter 2.

The fourth is *surgical exploration* where there is doubt. Diagnosis in the late stages is easy but is unavailing for treatment. In the late stages of malignancy, treatment is at best only palliative. In the early stages the surgeon may be in doubt during the operation. Frozen sections are made and they help to guide him.

Prognosis

The fate of a patient with carcinoma depends upon various factors but principally upon the degree of dissemination. If the growth is local it can be removed or irradiated with hope of a cure; if it has invaded adjoining tissue or lymph glands, it is less hopeful; and if it has spread to distant tissues, or lungs, it is hopeless. Another important consideration is the location of the growth—not only from the standpoint of early diagnosis, but from that of surgical extirpation as well. MacCarty has listed the following factors in the order of their importance:

1. The presence or absence of glandular involvement and distant metastasis.

2. Fixation of the growth, making its complete removal more difficult.

3. Location. If in a situation easily accessible to examination and treatment, early diagnosis and cure will follow. The reverse is true.

4 and 5. Renal and cardiac efficiency. Their role in cancer is similar to their role in general health. If poor, the prognosis is not good, for the therapeutic risk is greater.

6. Anemia, due to reduction in diet, to loss of blood, or perhaps, to toxemia. The greater the anemia, the greater the therapeutic risk. This may not affect prognosis if the anemia appears suddenly and is counteracted by transfusion.

7. Size of the growth. The larger the primary growth, the greater possibility of glandular involvement; hence, the worse the prognosis (although size alone may be misleading).

8. Age. The younger the patient, the worse the prognosis, all other factors being equal.

9. Direction of growth. Cancers which grow toward the lumen of an organ have a better prognosis than those which grow outward, invading its wall, for the latter are more apt to result in granular involvement.

10. Loss of weight may be due to the quality or quantity of the food, mechanical obstruction, pain, worry, infection, or to the absorption of toxins from disintegrating tissues It is important only in connection with other factors.

matter of seconds. These and many other objections have brought us to adopt the following procedure: (1) Biopsies are taken with a separate set of instruments; (2) the defect thus created is closed by inversion suture; (3) instruments, gloves, and gowns are discarded while waiting for report; (4) small growths are completely excised because if benign the operation is over; (5) large growths have permeation of lymphatics which in turn have a perilymphatic fibrosis close to the edge of the growth; therefore biopsies are taken from this edge because the center of the tumor may be necrotic and therefore noninforming; the edge shows active invasion; (6) sarcomas are usually seen in the extremities and wherever possible a proximal tourniquet is used which is not removed if sarcoma is present, amputation being done proximal to the tourniquet. In sarcomas of the shoulder this is not possible (see Chapter 21). Biopsies are cut by frozen section (for immediate study) or by

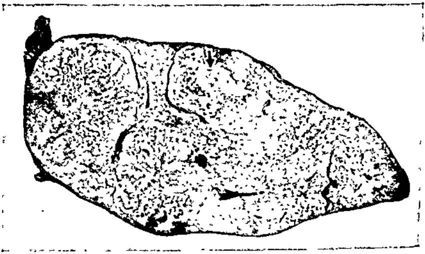

Fig. 128.—Metastatic areas in the liver in a patient with primary adenocarcinoma of the stomach. Woman aged 58 years. The specimen has been transected. The arrow points to one of three large nodules.

biconcave razor and stained with polychrome methylene blue (Terry's supravital technique). A study of biopsied tissue does not infallibly lead to the correct diagnosis and therefore all tissues excised are examined after paraffin blocks have been made and cut and special stains applied. However, the biopsy is an important aid in the diagnosis of new growths in the operating room.

Other aids to diagnosis are (1) the study of exfoliated cells from cancerous tissues by (a) vaginal smears in the diagnosis of uterine or vaginal carcinoma, (b) urethral smears and study of centrifuged urine in diagnosis of malignant neoplasms of the kidneys, ureters, and bladder, and prostate, (c) sputum smears and bronchoscopic washings in carcinoma of the respiratory tract, (d) gastric secretion obtained by aspirated fluid or through gastroscope, (e) exudates and transudates from pleural, peritoneal, and cerebrospinal fluid by making a "button" and

11, 12, 13, and 14. Cellular differentiation (the less differentiated, the more malignant); lymphocytic infiltration (prognosis better *with* than *without*); fibrosis (better with); and hyalinization (better with).

15. Duration of the disease. The history as to onset is often unreliable.

Treatment

If a growth can be completely removed, it is entirely curable. This statement holds true also if the related glands can be completely extirpated. It may be arbitrarily stated that the *best treatment is still radical and complete surgical excision.*

X-rays are useful in the preoperative control and aid postoperatively in the cure of cancer. It is perhaps true in some cases that x-rays used preoperatively seal the lymphatics and prevent dissemination, thereby increasing the efficacy of surgery. The postoperative irradiation, according to some, helps in the cure. Many groups of statistics seem to disprove this. This will be further considered under the various types of carcinoma, for radiosensitivity is an extremely variable factor and is useful in diagnosis as well as in treatment. (This is especially true of growths rich in immature cells, such as lymphosarcoma, Ewing's tumor, embryoma, etc.)

Radium has supplanted surgery in the treatment of certain lesions, such as carcinoma of the cervix and of the mouth. Coutard has shown that repeated small doses over a longer period of time are preferable to single large doses. Coley's mixed toxins are used in inoperable sarcoma. Repeated injections of *Bacillus prodigiosus and Streptococcus erysipelatis* may cause a disintegration of the growth with absorption. This may be explained by the reaction seen in the Arthus phenomenon. A great many nonoperative cures or recessions are associated with various inflammations. Many following incomplete surgery are due to asphyxia of the growth. Some recessions result from combinations of the above plus such chemicals as zinc and arsenic for reasons previously discussed. Lastly, a certain number of extensive carcinomas with incomplete surgery are helped by postoperative x-ray therapy because the induced (by surgery or infection) reaction is radiosensitive, whereas the original tumor may not have been.

Aids in the Treatment of Cancer.—

Androgens. Testosterone acetate and *proprionate* are useful in mammary carcinoma in women to relieve pain and delimit spread. The usual dose is 25 mg. every other day. Oophorectomy as an aid in treatment of breast cancer is doubtful.

Estrogens. Stilbestrol is very useful in the treatment of carcinoma of the prostate gland with or without metastases, causing a gain in weight, relief of pain, reduction in size of enlarged nodes and of the prostate. Serum acid phosphatase levels are decreased. The dose is 5 to 10 mg. daily. Orchiectomy is very helpful.

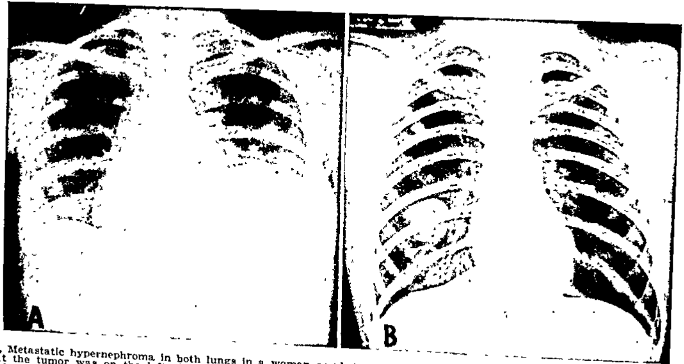

Fig. 129.—*A*, Metastatic hypernephroma in both lungs in a woman aged 41 years. There is elevation of the left leaf of the diaphragm due to the fact that the tumor was on the left side. *B*, Pulmonary metastasis from fibrosarcoma of the leg. Single metastases of this type may be treated by lobectomy after the primary lesion has been removed. We have removed a lobe of the lung in metastases from hypernephroma, fibrosarcoma of the leg, adenocarcinoma of the sigmoid. All patients recovered but ultimately succumbed to the disease except the last. This woman is alive and without recurrence three years after lobectomy and seven years after the colon resection.

Fig. 131.—*A*, Metastatic lesions of the pelvis, femur, and spine, due to cancer of the breast. These may be single or multiple and may show destruction, or (rarely) local areas of increased density. *B*, Metastatic nodules in the pelvis due to carcinoma of the prostate. The iliac crests are not shown; they presented a typical moth-eaten appearance.

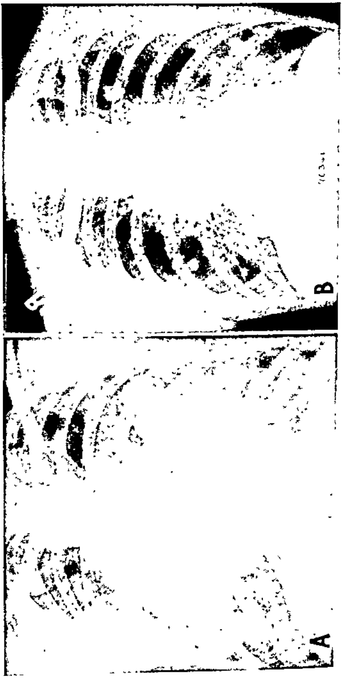

Fig. 130.—*A*. Extensive metastases to the lungs from teratoma of the testis. *B*. Metastases to the lungs from carcinoma of the breast.

obstruction is sudden but far removed from the organ (as low in the ureter), then all of the organ will not be involved at the same time and moreover some parts of it will derive a blood supply through collateral circulation and instead of atrophy there will be dilatation of the proximal parts of the ducts with cyst formation due to distention and pressure atrophy immediately around the dilated duct. Examples of this are seen in hydronephrosis especially from vesicle neck obstruction due to prostatic hypertrophy or ureteral stone and in carcinoma of the head

Fig 132—Thyroglossal duct cyst. The cavity was injected with methylene blue and excised.

of the pancreas with distended gall bladder which dilates before intrahepatic duct dilation occurs. Even the stomach becomes enormously dilated with resulting thin walls from intermittent complete obstruction as seen in ulcer or polyp. Partial obstruction usually leads to hypertrophy in all examples given. It is the muscular elements which are responsible because these force the secretions out through the constricted but not occluded duct.

Infection may alter any effect of obstruction, having its characteristic destructive action leading to infected hydronephrosis, thick-

Isotopes. Radiophosphorus has been used in leucemia, lymphosarcoma, polycythemia vera, myeloma, Hodgkin's disease, and metastatic carcinoma. Results are doubtful. Given orally the dose is usually 1 to 2 millicuries per week for several weeks. As much as 100 millicuries per kilogram of body weight have been used as the total dose. *Radioactive iodine* has been used with encouraging results in carcinoma of the thyroid and in metastatic carcinoma of the thyroid. Other isotopes are radioactive iron, sodium, potassium, chlorine, bromine, calcium, strontium, sulfur, carbon, and hydrogen.

Nitrogen mustard methyl bis (2-chlorethyl) amine hydrochloride has been used in daily dose of 0.1 mg. per kilogram of body weight given intravenously for the control of lymphoblastic diseases. Results have been equivocal.

Stilbamidine (4,4′-stilbenedicarboxamidine), ethylstibamine (Neostibosan) and *urethane* has been tried in leucemia and metastatic carcinomas. Stilbamidine ethyl carbamide is given orally, intravenously, or intramuscularly daily in doses of 0.5 to 2 Gm. There have been reports indicating relief of pain.

Other chemical agents which should be mentioned as still in the early experimental stage are *Serratia marcescens (Bacillus prodigiosus)* polysaccharide; KR (carcinolytic substance of *Trypanosoma cruzi*, named after Klyueva and Roskin); antireticular cytoxic serum (ACS); folic acid antagonists such as aminopterin (4-amino-pteroylglutamic acid) and amino-an-fol (4-amino-pteroylaspartic acid).

CYSTS

A *cyst* is a swelling consisting of a wall and fluid or semifluid contents. It usually results from the distention of pre-existing ducts or spaces, or from new growth.

Cohnheim studied the effects of complete obstruction of the principal duct of a secreting gland. This usually produces atrophy of the organ. The retained secretion or excretion increases under pressure (glands will secrete or excrete against a pressure gradient) which finally equals the venous pressure of the organ. When venous pressure finally equals arterial pressure, cellular degeneration and necrosis results from asphyxia; then there is absorption through surrounding lymph and blood capillaries of tissue debris, with final fibrosis and atrophy. Examples of this are seen in kidney atrophy and fibrosis after sudden and complete ligation of the ureter and in liver atrophy and cirrhosis after accidental ligation and division of the common bile duct. Obviously the first effect is an increase in size of the organ due to retained products and passive congestion; the end stage is atrophy.

These effects are variable depending on other factors, principally infection and pressure gradients. The latter will be considered first. If the principal duct is slowly and/or intermittently obstructed or if the

2. Epidermoid cysts. Surrounded by squamous epithelium with smooth walls or pearly granules containing clear fluid.

3. Blood cysts (hematoma). May be due to endometrial transplants.

4. Cysts due to foreign bodies which become encapsulated; also parasitic cysts, as echinococcus cysts.

5. Cystadenoma. The proliferating papillary cystadenomas have malignant tendencies in the ovary and breast.

6. Cystic degeneration may occur in any new growth.

7. Transplantation cysts. Due to epithelial transplants at operation or from injury. (Acquired dermoid or epidermoid cyst; also cystadenomas may be transplanted at operation into peritoneal cavity and vagina in panhysterectomy; endometrial transplants at operation or spontaneous.)

8. Inflammatory cysts. Result from an infection untreated with destruction of cells and abscess formation. Liquefaction of pus and filling of dead space with serum surrounded by scar. The wall is scar tissue.

Diagnosis

The diagnosis of a cyst is made from its transmission of light, its fluctuant quality, and its position. In case of internal cysts, a sense of resiliency is palpated, and the position (usually ovary) makes the diagnosis possible.

Treatment

Retention cysts are treated by excision of the cyst wall so that they may not re-form. Sometimes cysts are cured by the injection of sclerosing agents or spontaneously due to infection and inflammation.

Where the cyst involves an ovary, the ovary is usually removed (except in the case of a follicular cyst) because many cysts are new growths and may lead to malignancy. Endometrial cysts are treated by excision. If many transplants are present (endometriosis), ovarian function is destroyed by x-ray or surgical castration.

In the case of cysts due to parasites, the cyst wall and the daughter cyst must be carefully removed if that is possible; if not it is chemically destroyed. This is a rare state.

In general, the treatment of a cyst is the removal or extirpation of the cyst wall. This is usually feasible. In hydrocele, the tunica vaginalis is simply everted. Sometimes the wall of a cyst is marsupialized (as in mediastinal dermoids and pancreatic cysts) although here extirpation is preferable if possible. In extravasations into pre-existing cavities, aspiration is sufficient, because the wall of the normal cavity will assume its power of secretion and absorption when the disease process causing it ameliorates (pleurisy with effusion, hematocele, hematocolpos, etc.).

In this chapter we have discussed, in a general way, the subject of tumors and cysts. It remains now to review the manifestations of these growths in their respective organs and tissues and finally to describe their treatment. This will be done in succeeding chapters.

ening and decrease in size of the gall bladder from common duct stone, etc. Conversely, obstruction to an excretory duct is perhaps the most important *cause of infection in an organ.*

Classification of Cysts

Distension Cysts.—

1. Retention cysts *(congenital or acquired) are due to obstruction of* the duct of a gland and may occur in sebaceous glands (wens), the salivary glands (ranula), the breast, the pancreas, the kidneys, etc.

Fig. 133.—Dermoid cyst. This is a common site. The cyst was excised.

2. Exudation cysts are due to an accumulation of fluid in a pre-existing cavity *(ganglion of tendon, hydrocele, etc.).*

3. Extravasation cysts are due to hemorrhage in a pre-existing cavity (hematocele cysts, etc.).

4. Congenital cysts are due to anomalies of the lymph spaces or to failure of an embryonic cavity to close *(cystic hygroma of the neck* [lymph], branchial cleft cysts, thyroglossal duct cysts, mesenteric cysts, etc.).

Cysts of New Formation.—

1. Dermoid cysts (in skin, ovary, testes). May contain *epidermis,* dermis, and dermal *glands.*

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PART V

DISEASES AND INJURIES OF SPECIFIC ORGANS AND SYSTEMS

In foregoing chapters we have outlined the general principles involved in the causation and response to injury. In the remaining chapters of the book we shall consider these principles as applied to particular organs and systems.

It is difficult to follow a definite outline in all instances. However, a convenient method of presentation includes the following studies: (1) Embryology, (2) Anatomy (Gross and Microscopic), (3) Physiology, (4) Abnormalities. The latter may be considered under the following heads: I. Functional disorders, which may be motor, sensory, secretory, circulatory, excretory, or combinations. II. Organic changes due to (a) Congenital malformations, (b) Traumatic injury, (c) Infections and inflammations, (d) Neoplasms, (e) Miscellaneous causes including diminished or increased blood supply, obstruction to principal duct from various causes, calculi, etc. III. Combinations, functional derangements leading to organic changes (such as Raynaud's disease, tumors of endocrines, etc.), the reverse of which is usually the case. *Wherever possible the disease will be presented under the following* heads: etiology, pathology, symptoms and signs, diagnosis, prognosis, and treatment.

Lastly, where surgical operations are indicated, a brief discussion of preoperative preparations, operative technique, and postoperative care will be considered as applied to specific procedures.

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baceous material, and, as we have seen, it plays an important role (in man) in the regulation of the body temperature, the water balance, and chloride metabolism. It is provided with numerous accessory organs such as hair, nails, sebaceous glands, and sweat glands. Hair is present in at least a rudimentary form over the entire body except on the flexor surfaces of the hands and feet, the dorsal surfaces of the terminal phalanges, the glans penis, the inner surface of the prepuce, and the medial surfaces of the labia. Sebaceous glands occur with the rudimentary hair follicles, and therefore areas which are devoid of external hair may have boils, carbuncles, and sebaceous cysts. This does not apply to the regions mentioned that are entirely without even the rudimentary follicle (the lanugo of the fetus). The dog has few sweat glands; consequently he must regulate body temperature and fluid loss through the respiration, the kidneys, and the bowel.

Immunity

Koch's rapid strides in bacteriology influenced many of his time to believe that "the individual has no more resistance to bacteria than a soldier to bullets." However, Ehrlich clearly demonstrated that there are humoral substances which he called antibodies to fight bacteria and their toxins (agglutinins, precipitins, antitoxins, bacteriolysins, alexins, opsonins, hemolysins, etc.). Later, Metchnikoff showed the value of phagocytic cells in local immunity (macrophages, reticulo-endothelial cells, etc.). Today we believe that both play an important role, with perhaps local immunity the more important of the two.

The skin possesses a high degree of *immunity*. This must be true since it is in contact with bacteria at all times. We have seen that even after careful surgical preparation the skin harbors bacteria in the hair follicles, sebaceous and sweat glands, horny fat, crypts, and crevices. Recent studies seem to show that bacteria are found in most tissues of the body. They are not always pathogenic for experimental animals unless they are incubated. It is important to know these facts since the entire problem of skin infection hinges upon it. If the skin is not devitalized by trauma or strong chemicals, and if the general condition of the patient is good, infections will not occur when reasonable cleanliness is exercised. Resident bacteria are mostly *Staphylococcus albus*. They cannot be entirely removed by scrubbing or strong antiseptics. In fact, preoperative scrubbing done the night before surgery increases the flora which becomes less after five to six days. Therefore we do not scrub the operative field the night before surgery.

Inflammatory reaction in the skin is in the dermis and hypodermis rather than in the epithelial cells which apparently have no defensive or phagocytic powers. They respond to irritation by degeneration or disintegration, as in hyperkeratosis or leucoplakia, or by hypertrophy and hyperplasia, as in condyloma formation. In early carcinoma the

CHAPTER 16

THE INTEGUMENTARY SYSTEM AND ADIPOSE TISSUE—SKIN, NAILS, HAIR; SEBACEOUS GLANDS, SWEAT GLANDS, MAMMARY GLANDS

INTEGUMENTARY SYSTEM

The skin forms a covering over the entire body and in a modified form, as mucous membrane, lines the body cavities. It is ectodermal in origin (see Chapter 3 for embryological considerations) and histologically is called stratified squamous epithelium.

The skin is composed of two layers. The outer layer is known as the epidermis and the under layer as the derma or corium. The former is composed of (a) the stratum corneum, (b) the stratum lucidum, (c) the stratum granulosum, and (d) the stratum germinativum (Malpighian layer). The derma or corium is composed of (a) the stratum papillare and (b) the stratum reticulare. The skin also contains sweat and sebaceous glands (which connect with the outside) and hair follicles. Elastic fibers roughly follow these hair pits. The hypodermis is subcutaneous tissue.

The normal integument is covered with valleys (sulci) and ridges (cristae). In a rough way these show the lines of the elastic fibers. If wounds occur or incisions are made parallel with these fibers, the scar will be narrow, with minimal deformity, whereas if they cut across the fibers there will be separation of the wound margin and increased scar formation (see Chapter 3). The most important layer of the epidermis is the lowermost (the stratum germinativum) for it is chiefly from this layer that new cells are made. Consequently, if in burns or wounds this layer is destroyed, a scar is sure to form (see Chapter 6).

Blood and lymph vessels are carried in loose connective tissue into the stratum papillare and from here they penetrate the lower layers of the epidermis as far out as the stratum granulosum. The capillaries are seen as small loops, and the lymph vessels end as small blind sacs, forming a meshwork comparable to a layer of mesh gauze in the epidermis. These lymphatics are known as the reticular lymphatics and they in turn go down connective tissue columns to empty into the large lymph vessels which lie on the deep fascia (tubular lymphatics), which in turn empty into anatomically related lymph nodes. Such infections as erysipelas and tubular lymphangitis involve these structures.

The skin protects the organism from injurious external influences, it receives sensory impulses from the outside, it excretes water, salt, se-

lent from the start (that is, full of polymorphonuclear leucocytes). In both infection and injury the forces of repair are at work. However, they cannot succeed until local immunity is established. This is true because the toxins destroy granulation tissue as fast as it may be formed. Therefore, immunity and inflammation are not the same thing, and although inflammation is necessary to secure repair, the former does not guarantee the latter.

Repair is said to occur by *first intention (per primam)* if a minimum amount of granulation tissue is necessary. A clean cut made by a sharp instrument produces a minimum of trauma and if not accompanied by infection heals by first intention. At first blood from the capillaries and arterioles exudes in the wound. In about four or five minutes this clots. Fibrin is deposited and forms a "scaffold" for the exudate (plasma) which begins to be poured out within thirty to forty minutes. Therefore, there is swelling. Microscopically, this exudate is seen to contain blood plasma, macrophages, polymorphonuclears, some lymphocytes, endothelial cells, and later (about the fourth day) fibroblasts which become fibrocytes. The activities of these cells are to (1) fight invading organisms which are always present; (2) remove debris (macrophages, reticulo-endothelial cells, histiocytes, pericytes); (3) form capillary loops (endothelial cells); and (4) form collagen from which connective tissue ultimately develops (fibro blasts). The polymorphonuclears come from the blood stream, the macro phages from the blood stream and tissues (tissue wandering cells), the endothelial cells from the cut ends of capillaries and perhaps from histiocytes, and the fibroblasts from tissue spaces or histiocytes. The endothelial cells form in rows, which later become canalized. The entire mass of soft purple tissue is known as granulation tissue. It is a living structure, filled with immune bodies and capable of repairing a defect. On the surface of the incision the plasma has formed a crust. This is impermeable and distinctly bactericidal and is a better dressing than the surgeon could make. Under this crust the epithelial cells creep across on the granulation tissue covering the defect. Later the connective tissue contracts, squeezing blood out of the now useless capillaries and the scar contracts. The repair tissue is sufficiently strong to withstand slight tension within seven days and in two weeks is fairly firm. After six months the scar is bleached and contraction has occurred in each direction. In healing by first intention contraction is minimal (Chapter 3).

Healing by second intention requires the same forces. However, this type usually follows infection or denudation of a large area. Much granulation tissue is required and after immunity is established this fills the defect (healing from the bottom up). If excessive, it is commonly known as "proud flesh." As soon as this is accomplished, epithelial cells begin to grow in from the epithelial border of the wound. They are seen grossly as a delicate gray membrane. If the defect is not too large, they will ultimately cover the area. (This border should not be irritated or

hyperplasia is a disorderly attempt to repair damage to cells. In inflammation the skin does retain water and if slightly irritated protects itself in part by blister formation (see Chapter 6—Thermal Injuries).

In all *infections* there are two factors to be considered: (1) the invading organisms, and (2) the resistance of the host. Although the skin is contaminated at all times, infection does not occur unless the defense mechanism is impaired. The mere presence of bacteria does not constitute an infection. When infection occurs, nature clearly shows us by pathological and clinical signs: locally, by hyperemia and exudation (which are manifested *clinically* by heat, redness, swelling, and pain); and *systemically*, by fever and leucocytosis.

Usually ordinary street wounds are contaminated by various strains of bacteria. They are not present in large numbers if the wound has been unmolested. Should infection result, in most instances it will be due to a mixed infection, and therefore clinical signs and symptoms will not be true to any particular type. The site of the injury may play a role, for example: oral, usually mixed streptococcus and staphylococcus; abdominal, the intestinal flora, etc. This indicates that often the infection which may result is endogenous. As a rule, however, there are three chief kinds of infection seen after accidents. First, there are those caused by skin staphylococci (*Staphylococcus pyogenes aureus* and *Staphylococcus albus*) and giving rise to a localized type of inflammation. Second, there are those induced by streptococci (*Streptococcus pyogenes* and *Streptococcus hemolyticus*), a more serious type which gives rise to a spreading or diffuse type of inflammation (phlegmon). Lastly, there are infections by the anaerobic group, *Clostridium perfringens* (*Bacillus aerogenes capsulatus*) and sporogenes (*Bacillus edematis maligni*) and *Clostridium tetani* (*Bacillus tetani*). These are very serious and occur usually in punctured or badly devitalized wounds where oxygen is absent. The formation of gas and the wide destruction of tissue have given rise to the name gas gangrene. Not all collections of gas in the tissues are due to the Welch bacillus. Anaerobic bacteria normally inhabit muscle. They are nonpathogenic. Gas in the tissues without marked symptoms is seen after simple fracture, contusions, and injections of adrenalin in doses sufficient to produce local devitalization. Careful observation of clinical symptoms and signs is necessary to differentiate this from the more severe types. The indigenous anaerobes may become pathogenic in the presence of streptococci. After destruction of the skin, either by trauma or infection, nature attempts to heal or repair the defect. As we have seen, inflammation is nature's way of mobilizing its immunizing forces to combat infection or injury. In infection, these forces are chiefly concerned with fighting the invading organism until it is annihilated or (what is perhaps a truer statement) of making the tissues at the site of invasion (and if necessary, the body as a whole) an unfavorable place for bacteria to grow. The exudate in this case is puru-

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destroyed with silver nitrate, as is sometimes done.) The more granulation tissue, the more connective tissue and the greater the contraction; therefore, the more noticeable and deforming the scar.

So-called *healing by third intention* implies the union of two surfaces covered by granulation tissue which are brought together by sutures (delayed or secondary closure) or adhesive after local immunity has been established. This was first practiced during World War I (1914-1918). It is a useful way of shortening healing time and was used in World War II purposefully in badly contaminated wounds.

Traumatic Injuries

A *wound* implies a break in continuity of the skin which may be microscopic in size. However, as has been shown in Chapter 14—Shock, trauma may be applied in such a way that the skin is unbroken, yet severe hemorrhage may occur beneath it. There may even be rupture of a solid or hollow viscus without any sign of skin injury. Therefore, every contusion to any part of the body deserves careful study.

Wounds may be produced by a mechanical force, by thermal agents (heat or cold), by chemicals, by electrical discharges, and by x-ray or radium (Chapter 6). Those produced by mechanical forces may be divided into the following:

1. *Incised* wounds are those which are inflicted by a cutting edge such as a piece of glass or a knife. It is the kind that we produce in surgery. It heals most readily. It will probably remain uninfected longer than any other type of wound. It often heals by first intention if let alone and put at rest. Conversely if traumatized by strong antiseptics or rough surgery under the guise of débridement it may be converted into a contused wound. The eight-hour period within which a wound may be sterilized will vary with the kind of wound. Very few *wounds are primarily contaminated.*

2. A *contused* wound is one that is produced by blunt force. Sometimes there is sufficient trauma to destroy the skin; usually there is a break in continuity of the skin. It does not heal as readily as an incised wound because the tissue around the wound is devitalized.

3. A *lacerated* wound is one due to a tearing force. This heals slowly but not as slowly as the devitalized wound. Surgeons will often trim the frayed edge which is mostly dead tissue (débridement), thus converting it into an incised wound.

4. A *punctured* wound is one that is produced by a sharp-pointed instrument. Such a wound is the result of a needle, or a nail, or a stab wound produced by a knife. It has one great danger. It seals itself, producing an anaerobic medium favorable to the growth of *Clostridium perfringens, sporogenes* and *tetani.*

5. *Gunshot* wounds are punctured wounds produced by a bullet or shot. The bullet often carries pieces of clothing, etc., into the wound.

High velocity projectiles do not usually carry foreign material into wounds. However, this is unpredictable and therefore such wounds are carefully explored and débrided if necessary.

6. A *brush* burn is a superficial denudation of the skin.

The *presence* of a wound does not constitute an infection. If the area about the wound is thoroughly cleansed with soap and water for five minutes, using soft cotton, and if the wound is irrigated with copious amounts of physiological saline, infection is unlikely, provided this cleaning is done within six to eight hours from the time of injury. Soap solution is not a strong germicide but the mechanical scrubbing removes most of the transient flora of bacteria from the skin if continued for eight to ten minutes. Soap does not irritate the wound if it is washed out. It does aid in the removal of small foreign bodies, particles of dead tissue, and blood clot. Soap solution is weakest against staphylococci. Suturing *of skin wounds may be indicated if the injured tissue can be rendered* relatively free from bacteria; it is not indicated in wounds over ten hours old and may actually delay healing, except on the face, where the blood supply is excellent and local immunity is high. In badly contaminated or infected wounds delayed closure (five to six days) is preferable.

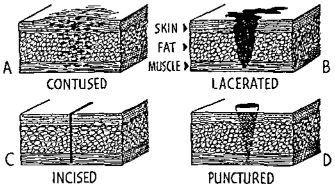

FIG. 134.—Diagram illustrating types of wounds. *A*. Contused wound produced by blunt force. There is great destruction of tissue. *B*. Lacerated wound produced by a tearing force. This results in an irregular wound with greatly damaged margins. *C*. *Incised wound produced by a sharp instrument.* *This* produces a minimum of trauma to tissue and healthy edges. *D*. Punctured wound produced by a sharp instrument. This seals itself quickly with serum and results in an excellent environment for anaerobic organisms.

As we have already seen, the less destruction of tissue, the less the possibility of infection, the smaller the area to heal, and, therefore, the more likely repair by first intention.

Obviously, then, an incised wound should heal better than a contused or lacerated one; that is, more quickly and with less scar. Punctured, gunshot, and stab wounds are dangerous because the wound is small and deep: it soon seals over, producing an anaerobic medium which is excellent for the growth of the *Clostridium perfringens, sporogenes* and *tetani*, and anaerobic streptococci. Brush burns are so very common that something must be said of their treatment.

Treatment of Wounds Produced by Mechanical Force.—*Arrest hemorrhage first.* This may be done by a tourniquet or by a tight bandage. If it is an extensive wound, the patient should be removed to a hospital. The wound is covered with sterile gauze and bandaged tightly. If an elastic bandage is available, it is applied. Many wounds which are relatively clean are contaminated by the first-aid attendant. Such contamination may be due to unclean hands, bacteria from nose and throat, washing the wound and surrounding tissue in such a manner that dirty water enters the wound, strong antiseptics, and rough handling. First-aid workers should be taught to cover the wound with a large amount of sterile gauze, bandage the part, and apply a temporary splint.

Then treat the patient as a whole for shock. This has been discussed in Chapter 14. However, a diagnosis as to the extent of the injury, the patient's general condition, and the presence of multiple injuries must now be made. Our experience in civil life has been the triple combination of head injury, abdominal or thoracic internal injury, and superficial skin wounds. In industry the hands are injured most. Lastly, one must be on guard for an injury in an individual who has had diabetes, a stroke, etc. When reaction has occurred, the wound should be treated. Let us assume that it is a lacerated and contused wound, filled with grease and dirt. The indications are clear and may be categorically stated as follows: (1) Control the hemorrhage by placing clamps on bleeders or leaving the tourniquet in place; (2) scrub thoroughly; this removes contamination and enables the surgeon to (3) make a careful inspection; (4) surgically remove any dead or devitalized tissue (débridement); (5) ligate the vessels and repair the nerve, muscles, tendons, and skin.

By *repair* we mean the restoration of continuity. This does not always mean functional restoration but may be only anatomic. Nor does it imply that repair will be made by like tissue. In general, the more highly specialized a tissue, the less its ability to regenerate itself. Of the five primary tissues, nervous tissue is perhaps most highly developed. Therefore, although the neurilemma of a nerve *fiber* may heal and the axis cylinder may grow down its sheath of Schwann if myelin is present, the cell *body,* if destroyed, will not regenerate itself. We have all the nerve cells we are going to acquire at birth; these may develop but will not increase in number nor regenerate when destroyed. Muscle tissue is also highly specialized and when it is destroyed repair takes place not by muscle but by connective tissue. Therefore, in sewing muscle, small amounts are included in the loosely tied sutures. Vascular tissue is partially able to regenerate. Epithelial tissue likewise is not entirely able to regenerate, for after the skin has healed there is an absence of sebaceous glands, sweat glands, and hair follicles in the scar. Connective tissue, the least specialized, is completely able to regenerate itself. (This includes tendon, bone, and cartilage.)

Various tissues contain special local characteristics which help healing. Local immunity is high about the anus and vagina and in the mouth. Therefore, although infection may occur, it does not greatly delay healing. The mesothelial tissues (pleura and peritoneum) heal very quickly (protective exudate composed of plasma fibrin is present within thirty minutes after an injury). The blood supply is also an extremely important factor in healing.

Perhaps the greatest factor in repair is the presence of normal, healthy cells. Anything devitalizing these will delay the process. However, there are other important factors: (1) *Infection.* This causes destruction of a wide area of tissue which is only healed after immunity is established, and then by second intention. (2) *Foreign bodies.* These must be removed. Grease, cinders, blood clots, wood, glass, hair, etc., are frequently closed within a wound. If a surgeon wishes to delay healing in part or in toto he introduces a packing or drainage tube. (3) *Blood supply.* The better the active exchange of oxygen and carbon dioxide and the more adequate the nutrition, the better the wound will heal. These processes are accomplished by an active blood supply. Sutures tied *snugly will produce anemia of the wound: allowance should be made* for swelling, which soon occurs. Tight bandages and casts are objectionable because they cut off the circulation. If the vessels are sclerosed (due to arteriosclerosis, thromboangiitis obliterans, or Raynaud's disease) healing will be delayed. At a site of complete occlusion healing may be impossible and there will be ulcer or gangrene. Stasis of blood may also retard healing. Asphyxia plus stasis may produce death of tissue. This is a result of occlusion of the venous return and is seen at its worst in Volkmann's contracture. In varicose veins there is stasis, accumulation of metabolites, insufficient oxygenation, and edema of tissue. Wounds do not heal in this environment. In the lower leg an elastic bandage with sponge pressure facilitates healing, especially in the presence of varicosities. (4) *Rest to the part.* A wound must be at rest to heal by first intention. This is the purpose of suturing the skin and of applying a cast in a fracture. Constant motion destroys granulation tissue and impedes its formation or leads to excess formation, thereby delaying repair; however, there is a possibility of the margins being too immobile. An extremity, for example, may be so thoroughly immobilized that circulation may be impeded. The stimulus of a very slight degree of motion may be important in bone repair. (5) The *size of the wound* may influence repair. Large denuded areas may be entirely healthy but the area may be too large for epithelization. This is seen after burns. Even if healing could occur it would be unwise to permit it. A vicious cicatrix would form, producing a crippling deformity. It it far better to apply split-thickness Thiersch or Wolfe grafts after granulations have formed. (6) The *general condition of the patient* affects repair—starvation, dehy-

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7. Tetanus antitoxin (5,000 units), or toxoid if the patient has been previously immunized, is given subcutaneously, and if the wound is badly contaminated, gas bacillus antitoxin is given in combination with it.

8. Besredka has claimed that anaphylaxis does not occur in patients under general anesthesia. However, in those with previous serum treatment or allergy, tetanus antitoxin is best administered in broken doses. The new tetanus vaccine now being used will greatly simplify the problem for the patient.

Accidental wounds are not often primarily contaminated; they may become infected when they have gone untreated for more than eight hours. In the stage of contamination, bacteria are lying on the wound surfaces and can be removed therefrom by mechanical means. In the stage of infection, bacteria have multiplied and penetrated the tissues so that their mechanical removal is no longer possible. It is obvious that the most favorable time for treating accidental wounds is in the period of contamination or six days later when local immunity is high and the process of getting bacteria out of the tissue hideouts will not be accompanied by their dissemination.

Reid quotes Billroth as follows:

> If you inject a drachm of putrid fluid into the subcutaneous cellular tissues of a dog, the result will be inflammation, fever, and septicemia. If you make a large granulating surface on a dog, and dress it daily with charpie soaked in putrid fluid, it will have no decided effect. On the borders of the new inflammatory formation the lymphatic vessels are closed; on the granulating surface there are no open lymphatic vessels, hence no reabsorption takes place.

The *treatment of contaminated wounds* should consist in the removal of as many bacteria as possible without inflicting any injury upon the tissues which can impair their power of resistance. No antiseptic has ever been devised which is not on the whole more injurious to leucocytes and tissue cells than to the bacteria. Antiseptics quickly lose their bactericidal power when mixed with body fluids. In fact, they make serum and blood a first-class culture medium. Tincture of iodine is perhaps the most dangerous antiseptic which can be applied to a wound. In contact with body juices it has a slight bactericidal action, and it injures the tissues with formation of scab under which bacterial growth can flourish with disastrous results. Fingers and hands are lost because of treatment of trivial cuts with iodine. If the cut finger be placed under running isotonic saline, the wound held open and thoroughly washed out, hemorrhage encouraged, and covered with a sterile, dry dressing, the wound will nearly always heal by first intention. Dakin's fluid is still used in infected wounds and burns. It is a poor antiseptic but it does increase exudation; however, at the expense of cell injury. Surface irrigation with physiological saline washes off transient contaminators and the subcutaneous injection (at a short distance) of the solution will infiltrate under the wound and cause it to weep copiously without cell destruction

dration, hemorrhage (due to low plasma or inadequate protein content), alkalosis, acidosis, or avitaminosis (as in scurvy and pellagra) interferes with wound healing.

If the injury is in an extremity, as is usually the case, the tourniquet may be left in place. This provides a bloodless field and enables the physician to clean and inspect the wound thoroughly. In any wound in which there is the slightest doubt concerning the depth or the injury to associated structures, general anesthesia should be used. If the wound is thoroughly cleaned within six to eight hours, infection is unlikely.

A method of sterilization which we have used with good results may be outlined as follows:

1. Aseptic surgical technique is employed (face mask, hands, and arms scrubbed for ten minutes; sterile gown) as for any major operation.

2. Gross cleaning. The skin about the wound is shaved and then is scrubbed thoroughly with soap and water and a soft brush. If grease or dirt is present, some cleaning agent is used. This should be a fat solvent (such as ether or carbon tetrachloride) or Boraxo, Sapolio, or other cleaner. Of course, such agents are irritating and should be thoroughly removed with sterile physiological salt solution. All visible foreign material is picked out.

3. Sterile towels are now placed widely about the area, and this is followed by irrigation of the wound with 1 or 2 liters of sterile isotonic salt solution. The surgeon puts on sterile gown and gloves.

4. All dead tissue is trimmed away and the flushing is repeated. Any filaments of tissue floating in the irrigating fluid are removed.

5. The tourniquet is released and all vessels are now carefully tied with chromic catgut, No. 00 or No. 000.

6. After change of gloves by the surgeon, tendons and nerves are repaired (see Chapter 3) and the wound is closed loosely by interrupted silk sutures. These should be simple (through-and-through) stitches and should be tied so loosely that there remains a gap of about one-fourth inch between the skin edges. If the wound is a deep and badly macerated one, or if it has been "washed out" by the untrained at home or if strong germicides have been used or if it is not treated until after eight hours, it should not be sutured. If the wound is first seen after twelve hours, infection is presumed to be present: no sutures are used, and the wound is left wide open until the danger of infection is over, five to six days, and then closed. In the latter instance, silk must not be buried in the tissues for it will act as a foreign body should infection develop. In the presence of an active infection it is best not to attempt the repair of tendons or nerves because suture lines may slough but to be content to secure drainage and remove loose foreign bodies. Rubber drains or gauze wicks are not used for they are foreign bodies. Wounds are either left open or closed loosely.

immunity is established the fracture is properly reduced and maintained. (See Chapter 21.) Joint cavities will heal if not traumatized. They should be irrigated with isotonic saline and closed. To leave them open results in infection and ankylosis—this is true even if the wound is old and if the primary wound is left open. Obviously if infection is already present the joint cannot be closed.

Nerve and tendon injuries sometimes are difficult to distinguish from each other. Cases have been reported of the inadvertent suture of one to the other. This may be avoided if a few rules are observed. The motor and sensory changes due to median, ulnar, and radial nerve injury in the upper extremity and of tibial and peroneal in the lower extremity are not hard to remember and offer characteristic signs (see Chapter 18). Tendon injuries are easily diagnosed by asking the patient to flex or extend the suspected tendon. At operation tendons retract and nerves do not. *If both are injured, the latter should be repaired first since they* usually lie deeper and there should be a minimum of handling of severed nerves after they have been repaired. Koch emphasizes the following principles: (1) gentle handling; (2) minimum of suture material—use fine silk; (3) protect line of suture with areolar or fatty tissue; (4) if the repaired tendon has a wide destruction of its sheath or if it is pulled away from its sheath, surrounding smooth parts of the sheath are brought over or fascia or tendon is secured from other parts of the body; (5) rest in splints in a position without tension for three to four weeks. (See Chapter 21.) Nerves are sutured with a minimum of fine silk. Knots are on the outside. Suture lines are covered by areolar tissue or fat or fascia so that adhesions do not form, and relaxation of paralyzed muscles is obtained by proper splints until reinnervation occurs. If a piece of nerve has been avulsed, end-to-end suture may be accomplished by freeing the nerve from areolar tissue of neighboring blood vessels above and below the site of injury, bringing the limb into flexion, transferring the nerve into a new position, as, for example, the ulnar from behind the medial condyle to the volar surface of the elbow. Nerve grafts may be tried and have been successful in extensive loss of substance.

After the deep structures have been repaired, the skin must be closed or covered with grafts. Koch lists the following rules for free grafts of intermediate thickness, free grafts of whole thickness, and pedunculated flaps when applied to the extremities:

(1) Use the simplest procedure that will give the desired results; (2) primary healing is desirable in a large wound which is always subject to infection; therefore a graft may be used which may not be ideal from the standpoint of appearance and function to get covering; later this may be replaced; (3) if the raw surface has a normal blood supply and if structures which require a covering of subcutaneous tissue are not exposed (tendons, nerves, large blood vessels, bones and joints), a free graft of intermediate thickness is best; (4) if the above structures are widely exposed so that they cannot be covered with skin and subcutaneous tissue from either side, a pedunculated flap from adjacent or distant tissue must be secured, because free grafts of skin and subcutaneous tissue are not apt to

or injury. If, in addition, sulfadiazine is given by mouth in the dose of 0.3 to 0.5 Gm. per pound of body weight as a prophylactic measure, infections will be rare. If the patient cannot take the drug by mouth, it may be given intravenously. Penicillin, 30,000 to 40,000 units intramuscularly every three hours, is added in badly contaminated wounds. Although many surgeons advocated the use of sulfonamides locally, our policy has been to avoid them because of their local irritating action (see Chapter 5). Penicillin has been used in low concentration (500 to 1,000 units per cubic centimeter) and is effective. In strong concentration it may be toxic for lymphocytes and leucocytes. Many antibacterial substances have failed as local chemotherapeutic agents because the complete pattern of requirements has not been met—that is, they are toxic, or they do not act in the presence of blood and pus or other environmental changes (iodine and mercury destroy surface bacteria and cells and create a favorable environment for bacteria to grow). Sulfonamides are slow, and they are inhibited by para-aminobenzoic acid and the presence of sloughs; they are toxic and act as irritants. Dry calcium penicillin is irritating but not so much as the sodium salt which is irritating in concentrations of 200 to 500 units per cubic centimeter. Penicillin is destroyed in the presence of gram-negative bacteria. Recently streptomycin has been used because it is effective against many gram-negative bacilli and some gram-positive organisms.

Having cleaned the wound, given antitoxins, and started chemotherapy, we turn our attention to the structures which have been injured and proceed with the repair.

In the *hands* one looks for injuries to blood vessels, bones, nerves, tendons, and joints.

When larger *blood vessels* are injured or torn, there is increasing swelling, discoloration, absence of pulse, coldness, and adventitious sounds in combined arterial and venous injury with venous engorgement. In this connection a word should be said about the removal of a foreign body which is buried or protrudes from the skin. In place there may be little sign of bleeding. When removed, an exsanguinating hemorrhage may occur due to the fact that the steel or wood piece has acted as a plug. All foreign bodies should be removed under general anesthesia with tourniquets on extremities and through a liberal incision to control bleeding by temporary occlusion of the principal artery or vein.

Injuries to *bones* and *joints* are not difficult to diagnose. Emergency treatment consists of the application of sterile dressings and splints, especially in compound fractures. In the hospital under aseptic conditions the wounds are cleaned, the fracture reduced, and the wound loosely closed if seen within eight hours. If not, the wound is left open, the fracture is reduced, and reduction is maintained by plaster cast. Six days later the wound may be closed. In very late and badly contaminated or infected cases, immobilization is secured by traction; then when local

Hidrosadenitis Suppurativa.—Hidrosadenitis suppurativa (acne conglobata, perianal pyoderma, axillary pyoderma, hydradenitis suppurativa, pyogenic granuloma, pyodermia, recurrent axillary or perianal furunculosis) *probably includes a number of closely related chronic inflammatory diseases of the skin.* The types which occur in the axillae, around the nipples, and in the inguinal, genital, and perianal regions are probably due to a chronic infection of the apocrine glands in these regions (see Chapter 22). These are specialized sweat glands located in the regions mentioned, giving off a characteristic odor. They may be involved in Paget's disease of the nipple and vulva. It is true that in most of the patients there is an associated diffuse acne vulgaris, multiple comedones, and sebaceous cysts. All of our patients have been men. The lesions may be limited to the axillae (axillary hidrosadenitis), the areolae of the breast (mammary hydrosadenitis), or the genital region. *Undoubtedly there is a constitutional predisposition to the disease.*

The lesions are notoriously chronic and are characterized by the formation of papules, pustules, large abscesses, chronic indurated sinuses, and a general fibrosis of the area. Patients are harassed by one abscess after another and by a continual drainage of pus. There is extensive undermining and burrowing involving wide areas which become progressively worse. The lesions resemble tuberculosis or fungus infections of the skin.

All sorts of remedies have been tried; namely, vaccines, x-ray treatment, local ointments and antiseptics, stilbestrol, sulfur baths, liver extract, Fowler's solution, low fat diet, and thyroxine therapy.

Excision of the apocrine gland-bearing areas and surrounding skin gives the best and quickest results. The fibrous and inflammatory tissue in the fat and connective tissue should also be removed. Then the entire area may be covered by skin flap shifts or split-thickness grafts.

Other bacterial diseases of the skin are as follows:

Infectious eczematoid dermatitis results from slight injuries, or scratches and is due to the staphylococcus as a rule. Often it is associated with ingrown toenails, furunculosis, and paronychia. It responds well to penicillin.

Impetigo contagiosa and other impetiginous infections are probably due to staphylococcus and streptococcus infection. The familiar blister and crust and spread of the disease is a common observation in any skin clinic. The treatment with penicillin ointment yields good results. Other forms of therapy include gentian violet solution, 1 per cent locally, silver nitrate, 10 per cent, and ammoniated mercury; adhesive tape over the lesions often results in early healing.

Systemic Integument Diseases

Many skin lesions are merely outward manifestations of systemic disease. These are considered elsewhere in the book. The *purpuras* are

take, and they would probably not give satisfactory functional results if they did; (5) whole-thickness grafts may be used in freshly made, clean, raw surfaces where a covering is needed that will not contract much, and will be thick enough for protection. Uniform pressure over injured tissues checks persistent oozing of blood and serum and it provides a substitute for the normal outer covering of skin and fascia.

Immediate skin grafts of all types should be used on extensive wounds seen within six hours which are too large to be covered by sliding flaps. Abrasive wounds may be covered after careful cleansing with split-thickness graft; finger tips, with full-thickness grafts. Wounds leaving exposed tendons need skin and subcutaneous tissue. This is often accomplished by a pocket flap from the anterior abdominal wall or thigh for the hand and a pedicle or pocket flap for the ankle, foot, or knee made from the other leg. Abdominal flaps created in the regions of the superficial epigastric artery and vein may be transferred by leaving only the inferior margin attached instead of attachment at both ends. This is possible because, as in scalp flaps, the blood supply comes from below and the flap gets ample nourishment through its inferior attachment. Full-thickness grafts taken from the neck and clavicular and postauricular and forehead regions have been found to give good results in the repair of facial defects; that is, eyelids, nose, and about the mouth. Although these donor sites afford little skin, it is usually enough for the defects mentioned. For the nostril border and tip and columella, two skin surfaces and cartilage between them are needed. The ear border is an accessible donor site which may be easily repaired after the graft has been taken.

Skin color is due to pigment and to the amount of blood flow. If it is necessary to take skin which does not match, pigment may be introduced for cosmetic reasons.

A good rule to follow is: use available tissue without graft if possible. This may often be accomplished by tissue shifting and rotation as in Z plastics or multiple Z plastics which are especially useful in freeing contractures or in the repair of excised scars (see diagrams in Chapter 3).

Wounds are not molested for at least eight days unless there is severe pain, bleeding, excessive exudation, progressive swelling, or severe systemic reaction. The part is immobilized and the patient should be put to bed if the wound is extensive. In less extensive wounds thorough scrubbing, careful removal of foreign bodies, and the control of hemorrhage are also important considerations. Sutures should be used sparingly if at all and introduced loosely. Rest to the part is imperative.

Skin Infections

Many of the ordinary skin infections have been considered in Chapters 5 to 9. More are beyond the scope of this book. There remain a few which are of interest to the surgeon which should be described here.

fibromatosis and tuberous sclerosis discussed below are also systemic afflictions. *Metastatic skin lesions and lymphoblastomas are often first* noted by nodules in the former and by mycosis fungoides in the latter.

Diseases due to fungi are discussed in Chapter 7. The surgeon is occasionally called upon to remove a toenail infected with tinea *(Trichophyton gypseum* and *purpureum);* the nail bed is then treated with x-ray. Protozoan diseases of the skin, of which syphilis is the most important, are discussed in Chapter 9.

Throughout the text reference is made to skin manifestations. This discussion is intended to show the interrelation of systemic disease with skin manifestations and the reverse.

New Growths in the Integument

Epidermoid Carcinoma of the Skin.—There are two main varieties of epidermoid carcinoma: (1) adult hornifying squamous carcinoma—acanthoma, *prickle-cell cancer, or spinocellular carcinoma and* (2) *basal-*cell carcinoma or rodent ulcer. Occasionally both varieties are present in a single lesion. A third variety is described by Ewing: transitional-cell carcinoma (lymphoepithelioma). It is seen over the tonsils, in the vault of the pharynx, in the nasal passages, at the base of the tongue, and in the nasopharyngeal tissues. It is infiltrating and involves lymph nodes early. The undifferentiated cells in this type of growth make it radiosensitive.

Squamous-Cell Carcinoma.—Squamous-cell carcinoma is often called rose cancer because of its elevated edges; it is seen on exposed parts such as the nose, lips, cheeks, eyelids, ears, and hands, and occasionally in old burned areas (Marjolin's ulcer). It is also encountered in the mouth, tongue, anus, and cervix and in these locations is more malignant. This growth is apt to occur at junctures of stratified squamous epithelium and the moist epithelium of mucous membranes.

When it occurs on the surface the growth is usually an ulcerative one with raised edges, while in the mouth it may be elevated as well. In general, the elevated variety is less malignant. In histological sections the cells may be seen breaking through the basement membrane into the subcutaneous tissues. Various stages of *epithelial cells are seen, some in* concentric whorls. The individual cells show intercellular bridges or spines, also keratinized areas (epithelial pearls). Forerunners of squamous-cell carcinoma have been listed by Eller and Anderson. Some of the more common are syphilis, leucoplakia, radiodermatitis, moles, senile keratosis, seborrheic *keratosis, kraurosis vulvae, occupational* keratodermias (tar, pitch, arsenic dust, oil, heat), lupus vulgaris and tuberculous cutis, lupus erythematosus, chronic ulcers (varicose, pellagrous, fistulous), Paget's disease of the nipple, cicatrices, cutaneous horns, Bowen's disease, extramammary Paget's disease, papilloma of the tongue, xeroderma *pigmentosum, blastomycosis, inflammatory* dermatoses

often associated with splenomegaly (Chapter 22). Xanthoma, cholesterosis, and other lipoid disturbances will be found in this chapter under Adipose Tissue. *Pellagra* is due to vitamin B deficiency, as is also cheilosis. *Scleroderma* is discussed with Raynaud's disease (Chapter 6). A more comprehensive view of diffuse scleroderma and also of *disseminated lupus erythematosis* is that of its involvement of collagenous tissues. The cause of scleroderma and of lupus is unknown. They may involve the connective tissue of such unrelated organs as the skin, esophagus, spleen, kidney, pericardium, and retroperitoneal and periarticular tissues; therefore they may be representative of a system disease—namely, collagenous tissue.

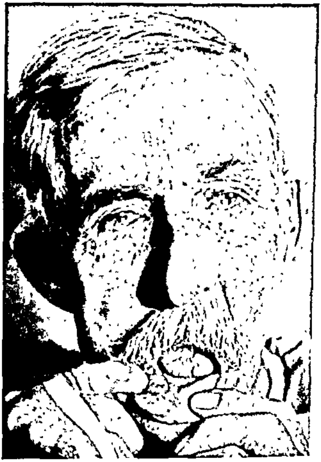


Fig. 135.—Early squamous-cell carcinoma of the lower lip in a man aged 70 years. There was lymphatic involvement. Complete excision resulted in a cure. (See Fig. 115.)

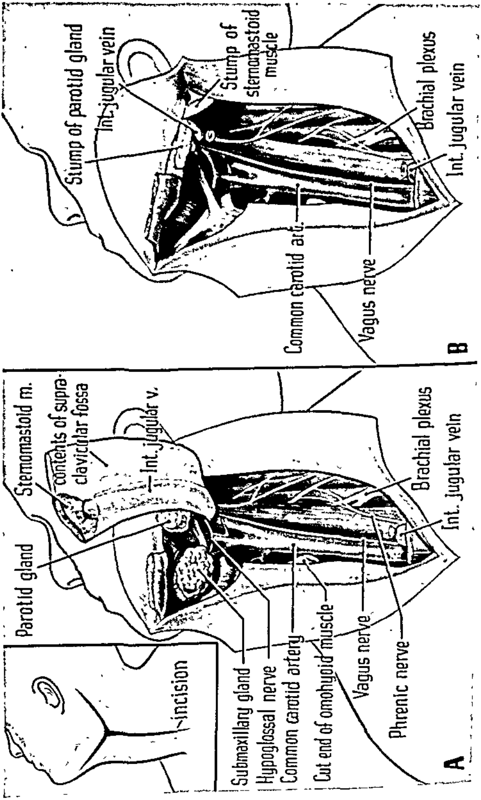
Another possibility is that they are primarily due to obliterative changes *in the smaller arterioles*. *Scleredema* is characterized by nonpitting edema of face, neck, scalp, conjunctivas, and thorax, rarely the extremities, and associated pleural, pericardial, and synovial effusions. Complete recovery usually occurs, and in this way, as well as in the changes in the lungs, esophagus, heart, and decalcifications of bones, it differs from scleroderma. *Dermatomyositis* is mentioned in Chapter 21 and it, too, may be a "system disease" of connective tissues. New growths such as neuro-

Fig. 136.—Diagram showing block dissection of the neck in carcinoma of the lower lip with metastasis. This is a logical operation because carcinoma of the lower lip rarely metastasizes below the clavicle. The dissection includes the removal of the submaxillary nodes, the submaxillary and a portion of the parotid gland, the lymph nodes of the jugular chain with ligation, and removal of the internal jugular vein. Carcinoma of the lip near the angle may metastasize to one side of the neck. This may also be true in metastatic carcinoma of the floor and roof of the mouth, tongue, buccal mucous membrane, cheek, and mandible. The nodes of the opposite side may be sampled for biopsy.

If both sides of the neck are involved, dissections are carried out on each side toward the midline and all structures removed en masse. The internal jugulars are not removed. The transverse incision is carried from one angle of the jaw to the other.

A. Insert shows incision for unilateral neck dissection. Skin flaps are made. The sternomastoid is divided near its sternal and clavicular attachment. The internal jugular is divided between double ligatures and the carotid sheath is dissected away. Fat and nodes are removed over the scaleni and trapezius. The posterior belly of the digastric and stylohyoid muscles is divided from the hyoid attachment. The submaxillary gland and its duct are freed after dividing the external maxillary artery and vein. The jugular bulb is found in front of the styloid process and is divided between double ligatures and removed. Then the upper end of the sternomastoid and digastric are divided near their mastoid attachment. The lower end of the parotid is removed.

B. Structures remaining after complete dissection. *The stylohyoid is erroneously shown to be intact.*


incision
Parotid gland
Sternomastoid m.
contents of supra-clavicular fossa
Int. jugular v.
Brachial plexus
Int. jugular vein
Submaxillary gland
Hypoglossal nerve
Common carotid artery
Cut end of omohyoid muscle
Vagus nerve
Phrenic nerve
A
Stump of parotid gland
Int. jugular vein
Stump of sternomastoid muscle
Brachial plexus
Int. jugular vein
Common carotid art.
Vagus nerve
B

the proximity of skin lymphatics. In the latter there is early involvement of the superficial lymphatics, thereby inducing a perilymphatic fibrosis; in the former the malignant cells are widely disseminated first and then the lymphatics are involved. The early surgeons called it *noli-me-tangere* (do not touch me) because of this fact. When diagnosed early it may be excised, but if seen late it should be treated by x-ray and radium for the best results.

Carcinoma (squamous or basal) in the mouth is best treated by radium, although if seen early, excision of the growth with a wide margin and dissection of anatomic glands may be done.

Fig. 138.—Late squamous-cell carcinoma of the lower lip in a man aged 40 years. Note involvement of submental and submaxillary glands. (See also Fig. 115.)

Squamous-cell carcinoma may arise on a basal cell. Therefore, a biopsy must be inclusive so that local excision may be accompanied by gland dissection if necessary. A second type of basal-cell carcinoma is really related to the dermal glands which it tends to reproduce. This is known as *adenoid epithelioma* of the skin. There are two main subdivisions of this group: (1) adenoid cystic epithelioma (Brooke)—multiple nodules of the face, neck, and chest in children at the age of puberty and (2) *simple adenoid epithelioma* seen in or near rodent ulcers. The former should be individually removed by excision or cautery when

(psoriasis, lichen planus, eczema). Clinically, it is first seen as a small scab or scale. This is picked off, leaving a small raw surface; then another scab forms, etc. Finally the ulcer remains and grows in size. In the lip it is frequently a small fissure and is usually on the lower lip. If untreated, it grows extensively, destroying even bone and cartilage. Metastasis occurs to the regional glands by embolism, not by permeation. It is *rarely seen below the clavicles although distant metastases have* been reported. It is important to remember that the metastatic area in the submental region may be the first evidence of a carcinoma of the floor of the mouth. Biopsies should be done only after a careful search has been made for the primary site of the cancer. Treatment consists in complete excision of the growth together with the affected glands. This implies a wide neck dissection. If on the face, in the mouth, or in the cervix, radium and x-ray are preferable to excision, but complete surgical removal of nodes and submaxillary gland should be done.

Fig. 137.—Basal-cell carcinoma of the face. (See Fig. 120.)

Carcinoma Basocellulare (Basal-Cell Carcinoma).—Carcinoma basocellulare (basal-cell carcinoma) occurs usually on exposed surfaces. The cells come from the stratum germinativum, are regular in size and shape, have no intercellular spines, and do not progress to the squamous or cornified stages of maturity. The growth begins as a smooth elevation and burrows down into the skin and laterally, elevating the edges. It may *destroy* bone and cartilage. It does not metastasize but will recur locally unless completely removed or destroyed. The reason for early metastasis in squamous-cell and none in basal-cell is thought to be due to

Melanoma Malignum.—Melanoma malignum (melanosarcoma or melanocarcinoma) is a very malignant growth of the skin (also of the eye and subungual region). It develops from the pigmented mole (an *atavistic remnant of hair feelers in lower animals*). *The chromatophore* or pigment cells of the skin are supposed by some to be of connective tissue origin and by others to be of epithelial origin. The growth may be started by a single trauma or by multiple or continued irritation. It grows very rapidly and metastasizes by the way of the blood stream and lymphatics, the glands becoming pigmented also. Death results from metastasis to the liver, brain, and lungs. The only treatment is prevention. A mole which is continually being traumatized should be excised with a small margin of normal tissue. X-ray is used without avail in the disseminated case.

Carcinoma of Branchial Cleft Rest.—Carcinoma of a branchial cleft rest is a rare type and is often confused with the more common lymphoblastomas described in Chapter 17. The tumor should be excised completely.

Benign Tumors and Cysts of the Skin.—

Hemangiomas and Lymphangiomas.—Hemangiomas and lymphangiomas are described in Chapter 17. Sometimes there is a combined hemangiolymphangioma. Myomas (dartoic and leiomyoma) are rare; also rare are chondromas which may be in the skin as rests and osteomas which may be confused with calcifications of inflammations and cysts. Some of the more common benign skin tumors and cysts are briefly described in the following paragraphs.

Wen or Sebaceous Cyst.—A wen or sebaceous cyst is an extremely common lesion. It is due to a plugging of the sebaceous gland duct, which fills with oily sebum, forming a cyst containing malodorous cheesy matter. The skin is usually adherent to the cyst but, as a rule, can be easily dissected loose. Sometimes it becomes infected and presents the picture of an acute abscess. In this case it must be drained. However, the only cure is the excision of the cyst wall. Cholesteatomas are closely related and are due to scaling and desquamation of epithelium. They are lined with stratified squamous epithelium and filled with sebaceous material and cholesterol crystals. They are seen in chronic mastoiditis and in the renal pelvis, brain, and hypophysis.

Dermoid Cysts.—Dermoid cysts occur in the skin and contain epidermis, derma, and dermal glands and structures (sebaceous material, hair, and even nails). They are probably best explained by Cohnheim's hypothesis. When they occur congenitally they are called *true dermoids* to distinguish them from *implantation dermoids* which result from traumatic displacement of epithelial fragments. True dermoids occur on the scalp, neck, back, median line of chest and abdomen, sacral region, and buttocks.

they show signs of growths because they are usually benign. The latter requires complete excision.

Bowen's Disease or Precancerous Dermatosis.—Bowen's disease or precancerous dermatosis is a chronic lesion of the epidermis which represents a specific form of precancerous keratosis. The lesions are multiple and pink or red and are covered with a thickened horny layer. The cells are irregular and anaplastic but hold to the base line and therefore the lesion has been called *intraepidermic carcinoma. Even after the rete* pegs have been traversed and carcinoma cells appear in the underlying tissue, they do not, as a rule, metastasize. Thus many squamous-cell carcinomas may be present over the body at the same time. This failure to metastasize has been attributed to the great fibrosis and lymphocytic infiltration about the lesions. The *treatment* is excision with related gland if they are involved—this is rare. Since so many areas must be removed, operations are done in stages so that too much denudation and plastic repair or skin grafting is not done at any one time. (See Figs. 116-119.)

Sarcoma of Skin.—Sarcoma of the skin may be primary, and take origin in the subcutaneous tissue and fascia (reticular sarcoma), or secondary. Fibrosarcoma, fibroma (not including keloids), lipomas, hemangiomas, lymphangiomas, angioendotheliomas, neurofibromas, neurolemmomas, lymphosarcoma, malignant melanoma, and metastatic carcinoma may occur in the subcutaneous tissue. Variations from benign fibroma to cellular fibrosarcoma occur and are easy to differentiate in extreme but not borderline cases. *Multiple hemorrhagic sarcoma (idiopathic multiple pigmented sarcoma of Kaposi)* is a special type starting with multiple lesions in the legs. These lesions start as bean-sized, reddish nodules with telangiectasis; soon the legs are greatly enlarged. Visceral involvement may cause hemorrhage, diarrhea, fever, and cachexia. The internal new growths are not metastases but are probably primary.

The histological picture is that of angioma with young connective tissue cells merging into definite sarcoma.

X-ray is the treatment of choice but is apt to be unavailing.

Lymphoblastic Disease.—Lymphoblastic disease is often accompanied by skin manifestations as exemplified in leucemia cutis, lymphatic leucemia, and myelogenous leucemia with skin lesions. Discrete lesions are those of lymphoma, lymphocytoma, Hodgkin's disease, and *mycosis fungoides* (granuloma fungoides). X-ray may give temporary relief.

Endothelioma.—Endothelioma of the skin is very rare. *Metastatic* lesions are not uncommon in late carcinoma. If the primary source is known, a nodule in the skin may settle the chance of operative cure. If the primary source is not known, it is well to withhold biopsy until an exhaustive search has been made; this is especially true in lesions about the mouth.

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Epidermoid Cysts.—Epidermoid cysts are congenital or traumatic, are usually filled with thin fluid, and are lined by a simple epidermal lining. They differ from dermoids in that there are no definite dermal structures. They may arise spontaneously or they may occur as a result of transplantation of epidermis by accidental injury or by downgrowth from a curetted ulcer. Rarely they are found on the palms or soles as a result of injury.

Branchial Cleft Cysts, Thyroglossal Duct Cysts, and Pilonidal Sinus.—These all represent developmental malformations. They are lined with epithelium and should be completely excised, including their cyst wall.

Wart.—A wart may be a true papilloma, or if there are multiple warts occurring in crops, they may be due to a filtrable virus. So-called "seed warts" are probably the former. For this type, excision or removal by cautery is best. The contagious types are often "aborted" by injecting

Fig. 139.—Pigmented nevus (mole). Benign. (See also Fig. 112.)

iodine or using x-ray. Soft warts may be simple folds of skin from unknown causes. A peculiar cauliflower type known as *condyloma latum* (venereal wart) may be due to gonorrhea or syphilis. It may be removed by the cautery or by nitric acid. Many of the venereal types disappear after the cure of the causative disease. Condyloma accuminata is due to any irritation which is prolonged. It represents a defensive reaction or degeneration of the skin. Podophyllin has been employed in their treatment; removal may be easier and quicker if only a few condylomas are present.

Mole or Pigmented Nevus.—A mole, or pigmented nevus, is a congenital malformation usually occurring in brunettes. Studies have been made of the nature and origin of two abnormal formations of the human skin, the lentigines and vascular moles. The lentigines of human beings are remains of tactile organs, which in earlier developmental stages had

the form of strongly pigmented warts, with tactile hairs; vascular nevi are enlarged sinuses that are the remainders of former tactile hairs. The histological examination of the nevus acanthosiformis suggests an atavistic formation dating back to the period of phylogenic development when the skin served as a respiratory organ; that is, to the amphibious stage. The mucus-secreting glands in cutaneous neoplasms are a proof of the amphibious ancestry of human beings. In members of the white race there occur nevi with and without hairs, while hairy nevi do not occur in Negroes. The skin of the white race developed from the skin of the amphibians by way of the land-inhabiting species with hairy skin.

Fig. 140—Plexiform neurofibroma of the face.

Negroes are free from hairy nevi because in the phylogenesis only one type of skin, that of the amphibians, is present. (Samberger.) Moles vary in size, shape, and color and may be flat or elevated. They should be excised if exposed to repeated trauma.

Fibromas.—Fibromas may occur as small hard nodules in the subcutaneous tissues. True fibromas are rare. The purest type is not regarded as a neoplasm but as an overgrowth of scar tissue *(keloid)*. A very cellular type, locally malignant, occurs in the flat muscles of the anterior abdominal wall, usually in young parous women *(desmoid, Zellreiches fibroma)*. It is an unencapsulated infiltrating fibroma of fascial

or aponeurotic origin with a *microscopic appearance which varies from* that of a fibroma to that of a cellular low-grade fibrosarcoma. The tumor should be radically excised, including muscle fascia and parietal peritoneum. Many desmoids are *radiosensitive and therefore x-ray therapy* may be used alone or postoperatively. We have seen two desmoids in men. Women should be warned against future pregnancies as the tumor is apt to recur following them. *Fibromas are commonly found in combinations,* as adenofibroma, fibromyoma, etc. In the skin they are usually associated with nerve sheaths—*neurofibroma* (in molluscum fibrosum and in Von Recklinghausen's disease). *These are slightly tender, hard nodules which* may occur anywhere on the surface of the body or in the brain (acoustic neuroma). Moreover, they are often associated with pigmented moles.

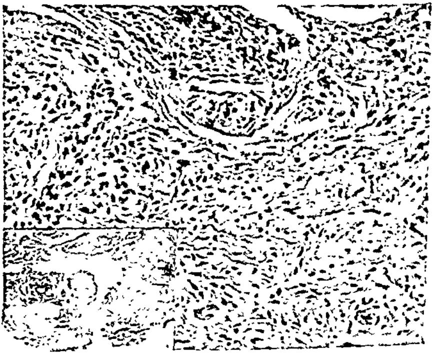

Fig. 141.—Neurofibroma of the face. Note the many nerves (left side of the low power) and the surrounding connective tissue. The high power shows nerves and fibromatous tissue.

Plexiform types *may* be very disfiguring. There is a definite familial tendency. A closely related tumor is the perineural fibroblastoma (Schwannoma or neurolemmoma) which grows from the *sheath of Schwann.* It *does not become malignant.* Treatment consists of excision of those growths which interfere with function.

Adenoma Sebaceum.—Adenoma sebaceum is seen in tuberous *sclerosis* (Epiloia) (tuberose sclerosis), a *syndrome* comprising epilepsy, mental deficiency, and adenoma sebaceum. There may be *congenital* enlargement of an extremity due to lymphatic obstruction; café-au-lait *spots* on the skin are common. Rarely there is splenic enlargement and in one of our cases a kidney tumor which proved *to be rhabdomyosarcoma* was pres-

ent. It is an ectodermal disease with cord changes and is related to neurofibromatosis. No satisfactory treatment is known.

Glomus Tumor.—A glomus tumor (glomangioma, angioneuromyoma) consists of a subcutaneous growth due to hyperplasia of the epitheliod or normal glomus cells. Normally there is an arteriovenous anastomosis in the skin of adults—not in infants. It is a coiled arteriovenous mechanism —Souquet-Hoyer canal. There is an afferent artery, then a coiled arterial organ, then a system of collecting veins; also preglomic arterioles with clear periglomic expansion zones furnished with neuroreticular mechanisms of sympathetic or myelinated nerves. Around the whole glomus is an outer lamellated collagenous zone. By this mechanism a large amount of blood can be quickly shunted into the skin to help regulate body temperature, local or general. The glomus mechanism is found chiefly on the digits, palms, and soles. Some are in the skin of the extremities and trunk.

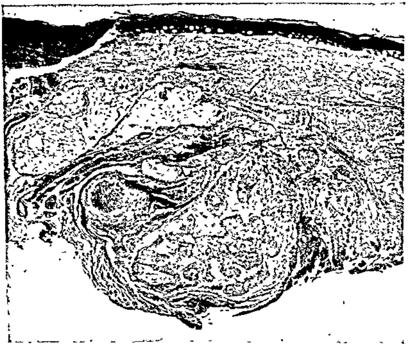

Fig 142.—Glomus tumor There are dilatation of the Souquet-Hoyer canal and hyperplasia of the cells surrounding the canal. These canals normally have smaller lumina but thicker walls than normal arteries, due to an increase in smooth muscle cells. The endothelial cells become cubold and the elastica fades out. Outside the muscle layer is the neuromuscular coat. The masses of cells in this tumor have been described as endothelioid, epithelioid, or a combination of nerve and muscle cells. The lesion is painful, due to pressure on nearby Pacinian corpuscles or on the nonmedullated nerve fibers within the tumor. Excision is curative.

Since none are found in infants, their body temperature cannot be regulated as easily. Clinically it is seen as a small growth which is extremely painful and is usually found on the extremities, often under the finger nails, and rarely, over the coccyx. The extreme sensitivity and pain are due to pressure on near-by pacinian corpuscles or the nonmedullated nerves it contains. The treatment is excision under local anesthesia.

ADIPOSE TISSUE

Eighteen per cent of the average person's weight is composed of adipose tissue. When fat is ingested, it is completely hydrolyzed during its stay in the intestine. The split into fatty acids and glycerine is the first step in absorption. Fat as such is rarely absorbed. Fatty acids are water soluble in the presence of bile. Fatty acids are transformed into phospholipids as an essential step in the resynthesis of fat. Insoluble fats are carried by the lymphatics to the blood—not to the liver. Cholesterol helps in this carriage and the blood plasma has neutral fat, phospholipids, and cholesterol esters. The liver takes an active part in fat transport. There is no doubt that some of this adipose tissue has a special function and is not merely connective tissue with fat cells.

Maximow doubted the origin of fat cells from fibroblasts and postulated their origin in part from undifferentiated mesenchymal cells about the blood vessels. Fat cells do not have the power to multiply—this is evidence of their high degree of specialization. (Wells.) There is ample evidence that some of it is glandlike in character. An illustration is the sucking-pad in the cheek. The primitive fat organ is closely related to small vessels and it originates from perivascular mesenchymal cells related to the reticulum. The fat organs, therefore, are formed from the same embryonic elements as the lymph nodes; that is, capillaries and reticulum cells of the vascular adventitia. This relationship is proved by the tendency for lymphoid tissue sometimes to replace fat tissue and conversely, as seen in the thymus. Also, the bone marrow is closely related to adipose tissue and this accounts for at least some extramedullary hemopoiesis. Adipose tissue may also be looked upon as a part of the reticulo-endothelial system. This is especially noticed in the omentum. When fat cells are distended with fat anywhere in the body, the organ in which this occurs need not necessarily be deficient in its function. This is also true of the individual fat cells. Very often the shrinkage of the organ necessitates a filling in of dead space, which the body will not tolerate, by fat. This is seen in atrophy of any organ in which there is a generous amount of fat deposit under the capsule of that organ. The importance of fat as a storage place for water is well known not only in the human being but also in the camel whose fatty hump is a water storage place and also in lower animals which hibernate. It is thought by some that essential vitamins such as vitamin C may be stored in this tissue. Therefore, it may be said that fatty tissue plays a role in water metabolism. Also, it has mechanical protective influence over important organs and tissues and it is also a factor in the regulation of body heat, for it is well known that the loss of heat through fatty tissue by convexion or radiation is less than over tissue not generously supplied with fat. Wells believes that adipose tisue may take on glandular function and may be intimately connected with glands of internal secretion. This is seen in cretins where glandular adipose tissue is found in the dorsocervical and interscapular regions until thyroid extract is administered. The perirenal fat in man exhibits some of the characteristics of glandular adipose tissue. The exact function of such tissue, of course, is not known. Adiposity in general may play an important role in the tendency toward disease and resistance (Chapter 10). Fat people are not, as a rule, good surgical risks.

Deposits of fat may vary in different parts of the body and have come to be known as: (1) general obesity due to dietary indiscretion; (2) that obesity which is general in distribution, particularly in the upper trunk, related to hypothyroidism; (3) that which is particularly noticed about the hips, related to pituitary disease; and (4) Steatopyga, bizarre strips of fat such as is seen in the Hottentot bushman type. General obesity may be an inherited characteristic or tendency. This is doubted by some who say the inheritance is environmental.

The various pathological deviations of fat aside from their distributions may be seen in lipomas, diffuse symmetric lipomatosis, as noted in Dercum's disease, adiposis dolorosa, and in Fröhlich's syndrome, dystrophia adiposa genitalis; also, in lipodystrophia progressiva in which the upper part of the body has lost fat, whereas the lower part below the waistline is generously supplied with fat. General obesity is another example of pathological deviations. Perhaps fatty tissue plays a part in general metabolism. This is exemplified by the interscapular fat organ's ability to convert carbohydrates into fat by way of glycogen deposits in fat cells. The presence of great deposits of fat in the cells need not interfere with normal metabolism of said cells since the cytoplasm is outside the fat and in close relation to the blood supply. There is no doubt that fat tissue is a part of the reticulo endothelial system and may play a role in immunity. When extensive fatty changes are produced in the liver and other parenchymatous organs by phosphorus and other steatogenic poisons, the fat, at least in part, comes from the adipose tissue depots, for extreme emaciation may interfere with the production of this fat metamorphosis. The disease of fatty tissue itself is seen in fat necrosis, both external and internal, the external type from the slight trauma as seen sometimes in the abdominal wall and the female breast and the internal type as seen following the presence of activated pancreatic juice in the abdominal cavity. Lipocaic, a hormone of the pancreas, is said to prevent fatty degeneration of the liver. Bile in the peritoneal cavity may produce necrosis, apparently through effecting tissue permeability so that enzymes escape from the pancreas. A disease known as sclerema neonatorum in which the adipose tissue becomes hard and rigid like chilled fat has been described. Sometimes this process is localized and the affected area may undergo necrosis even with subsequent calcification. This has been called adiponecrosis subcutanea neonatorum. The lipogranulomatoses are little understood and consist of a local necrosis of adipose tissue leading to tubercles formed by large numbers of lipophage cells and multinucleated foreign body giant cells. At times the fat is set free to form small oil cysts surrounded by a zone of macrophages and giant cells. These lipophage granulomas have been called tuberculids (Darier's and Bazin's induratum). They may become calcified. In addition, as has previously been mentioned, the role of fat in hypertrophy and atrophy of organs leads to replacement or disappearance when interference with the organ may occur. As an example of the former, the bone marrow fills in with yellow fatty marrow as opposed to the red marrow of early childhood, depending upon the need for blood cell formation. When bone is absorbed, its place is filled by fatty marrow. The heart and the pancreas may be so crowded by fatty tissue as to interfere with function. In chronic nephritis and pseudohypertrophic muscular atrophy, fat replaces the space left by shrinkage of the organ. It is suggested by Wassermann that in the fatty replacement of atrophic muscles the remaining capillary bed transforms itself with the intramuscular connective tissue into a new adipose tissue. In the common use of insulin for persons with diabetes there may be a localized melting away of the fat in the vicinity of the sites of injections. Nichols suggests that the concentration of insulin causes an active local combustion of carbohydrate which in turn causes active combustion of fat. Lastly, the diseases such as panniculitis or Weber Christian's disease, which is accompanied by attacks of fever or generalized lipoid necrosis of the subcutaneous tissue, is not explained as to cause. The process histologically resembles that seen in various forms of fat necrosis with inflammatory reaction such as is seen in traumatic fat necrosis. Gaucher's disease is also associated with disturbed lipoidosis and will be discussed in Chapter 22 under *Spleen*.

Specific Examples of Diseases of Adipose Tissue

Lipoma.—Lipoma is a tumor made of adult fat. It may occur anywhere in the body even where normally adipose tissue is not found (kidney, meninges, periosteum); however, it is usually found in the panniculus adiposus of the shoulders, back, and buttocks. We have

recently had a large retroperitoneal lipoma which protruded through the femoral canal. *Lipoma arborescens* is a multilobulated growth. Multiple lipomas are usually *neurolipomas*. Lipomas should be excised. This is usually easy if care is used to stay outside the capsule. Occasionally lipomas become malignant—liposarcoma—and reach an enormous size. There are two types, adult fat cell and embryonal lipomyxosarcoma. They should be widely excised. *Diffuse symmetrical lipomatosis* includes "fat neck" of Madelung, "adiposis dolorosa" of Dercum, dystrophia adiposa genitalis of Fröhlich. These may be related to pituitary gland dysfunction but this is not invariably so. In Dercum's disease there is often vasomotor instability, anhidrosis, hyperhidrosis which may be due to disturbances of sympathetic nervous system (see Chapter 18) and such trophic changes as loss of hair, pigmentation, and cutaneous ulcers.

Fig. 143.—Lipoma of neck.

Fat Necrosis.—Fat necrosis is usually focal. When pancreatic juice is released, as in acute hemorrhagic pancreatitis, the cleavage of fat by lipase is followed by soap formation and the deposit of small, white areas in the adipose tissue of the peritoneal cavity. It is the lipase rather than the trypsin which is responsible for the pancreatic fat necrosis. Pure pancreatic juice will not produce fat necrosis unless activated by intestinal juice or tissue kinases, and since the latter may be present at all times even bile introduced in the peritoneal cavity may affect tissue permeability so that pancreatic enzymes escape, causing fat necrosis.

Local fat necrosis is seen after trauma. In the breast this may resemble carcinoma clinically. A biopsy may be necessary to make the differential diagnosis.

Lipogranulomatosis.—Whenever fat is destroyed from whatever cause, proliferative reactions occur. Foreign body giant cells which are multinucleated appear as scavengers and there is tubercle formation with many lipophage cells. Sometimes there are oil droplets or cysts surrounded by macrophages and giant cells. Because of the nodular (tubercular) reaction these nodules have been termed *lipophage granulomas.* Bazin's erythema induratum and Boeck's and Darier-Roussy sarcoids are listed as tuberculids but may belong to lipogranulomas. These may become calcified. Erythema nodosum also causes skin nodules, especially in the lower extremities, and is related to rheumatic disease. It may be due to the streptococcus, to drugs, to syphilis, and to various other diseases. These lesions are transitory and should not be incised even though they may seem to be fluctuant.

Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian's Disease).—Relapsing febrile nodular nonsuppurative panniculitis is a disease of unknown etiology. The symptoms are recurring attacks of fever and subcutaneous inflammatory nodules over the body which regress, causing localized areas of atrophy. The microscopic picture is that of fat necrosis with inflammatory reaction. We have had one case which responded well to penicillin, 50,000 units, intramuscularly every three hours during the fever episode.

Xanthoma.—A xanthoma, or xanthelasma, is a tumor made of foamy cells which are yellow. These deposits, which contain cholesterol, are commonly seen under the eyes and are harmless but unsightly. They may be excised. More important is a disturbance of cholesterol metabolism which causes large deposits of cholesterol (in macrophage cells) in bones, tendons, and dura, with cholesterolemia. If associated with diabetes insipidus and exophthalmus, the condition is known as Christian's disease or Hand-Schüller-Christian's syndrome, a disease probably due to improperly metabolized lipoids and producing a cholesterin compound. Defects of the cranial bones are almost constant findings. Diagnosis is made by the following symptoms and signs: arrested development, complaint of pain on walking or a limp, diabetes insipidus, and exophthalmus. X-ray examination, bone biopsy, high blood cholesterol occasionally, and cutaneous xanthomas aid in establishing the diagnosis.

Gaucher's Disease.—Gaucher's disease (Chapter 22) is characterized by a disturbance of lipoid metabolism with anemia, splenomegaly, and hepatomegaly; the lipoid improperly metabolized is a *kerasin.*

Niemann-Pick's Disease.—Niemann-Pick's disease is a fatal disease seen in infancy, usually, though by no means invariably, in Jewish children. There is a brownish pigmentation of the skin, malnutrition,

retarded development, hepatomegaly, splenomegaly, decreased red cell fragility, leucocytosis, and generalized lipoid deposits. The lipoid improperly metabolized is a lecithin.

The Breast

Embryology

In early (8 mm.) embryos there is a thickening of ectoderm which extends ventrolaterally between the bases of the limb buds. This linear thickening is the milk line. In the future pectoral region of this line there is a downgrowth of the epidermis. From this downgrowth buds appear which elongate and form fifteen to twenty solid cords which become milk ducts. These branch in the mesenchymal tissue of the corium and will form later into alveoli. Externally they are covered by connective tissue. There is a lumen in the downgrowths except in the terminal swellings. Some of the cells which touch the connective tissue develop into basket cells of so-called myoepithelial nature. Where the milk ducts open there is a slight epithelial evagination which later becomes the nipple. In males the gland undergoes regression. In females the growth continues throughout childhood.

Anatomy

The breast is covered by skin, superficial fascia (panniculus adiposus), and strands of platysma (panniculus carnosus). The *superficial fascia* over the body is divided into (1) a fibroadipose layer (superficial) into which cutaneous nerves and vessels ramify and (2) a fibromembranous layer (deep) which is attached to the former. The deep layer in turn is loosely adherent to the deep fascia. In some areas of the body the superficial fascia is of great surgical importance. Colles' fascia in the perineum directs the course of urine extravasated from a ruptured posterior urethra, and the superficial fascia of the anterior surface of the thigh directs the course of a femoral hernia through the saphenous opening. In the mammary area the superficial fascia divides into an anterior layer, which covers the breast anteriorly, and a posterior layer, which lies under the breast so that the breast lies between the two. This is important because in abscess of the breast pus is prevented from involving the retromammary space and is directed anteriorly or around the periphery. These layers are closely approximated inferiorly and form a shelf which acts as a support for the breast. The posterior layer is attached to the deep pectoral fascia in the midline, and the latter is in turn attached to the periosteum of the sternum. Strands from the posterior layer permeate into the interlobular substance and are attached to the anterior layer—ligaments of Cooper. Lymph flow is directed along the ducts toward the nipple, peripherally in the anterior layer of the superficial fascia, and deep toward the chest wall along the strands of fibrous tissue to the lymph vessels on the deep pectoral fascia. Sometimes a bursa is found behind the breast.

The deep pectoral fascia, like the deep cervical fascia, also splits into layers which enclose the pectoral muscles; the anterior layer covering the pectoralis major is attached to the clavicle, sternum, and is continuous with the deep fascia covering the rectus abdominus and external oblique and laterally with that covering the serratus magnus below and deltoid above. Between these muscles the fascia forms the floor of the axilla. The posterior layer encloses the pectoralis minor, forms the costacoracoid membrane, continues under the clavicle, enclosing the subclavius muscle, and is inserted into the subclavian groove. These various layers of the posterior part of the deep pectoral fascia are known as the clavipectoral fascia. Pus or collections of fluid between the pectoral muscles are thus usually directed toward the anterior border of the axilla. If such collections occur behind the pectoralis minor (and therefore posterior to the fascia) they point at the base of the axilla or up above the clavicle.

In making a dissection of the axilla, the following muscles are encountered: anteriorly, pectoralis major, pectoralis minor, clavipectoral fascia (costocoracoid membrane); posteriorly, subscapularis, teres major, latissimus dorsi, and serratus anterior. The blood supply of the beast is from (1) perforating branches of the internal mammary, (2) external mammary branches of the lateral thoracic, (3) intercostals; the veins empty into the axillary and internal mammary. In the radical operation the following vessels are encountered: superior thoracic, thoracoacromial, lateral thoracic, subscapular, and also branches of the internal mammary and the intercostals. The veins are the same as the arteries. The cephalic vein which lies in the groove between the deltoid muscle and pectoralis major and thus demarcates the two muscles is a guide to the first part of the axillary artery because it empties into the axillary vein which overlaps the artery. The axillary vein is completely bared in the operation. The nerves are anterior branches of the intercostal, intercostohumeral, the long thoracic which supplies the serratus anterior), and the thoracodorsal (which supplies the latissimus dorsi). Sometimes in paralysis of the serratus the scapula falls forward, forming the so-called winged scapula (scapulae alatae).

Physiology

The lymphatics begin with disconnected reticular lymph capillaries which ramify the breast, and a special areolar network surrounds the nipple. These empty into the large plexus which lies upon the deep pectoral fascia. Here the principal channels are as follows: Along the axillary border of the pectoralis major into the axillary nodes—these are the first to be involved from carcinoma in the most common site, upper outer quadrant of the breast. From these, the nodes along the axillary vein are involved, and finally the subclavicular and supraclavicular nodes. Behind the pectoralis major on and under the clavipectoral fascia are lymph vessels which follow the superior thoracic, thoracoacromial, and external mammary vessels. These terminate in small nodes behind the pectoralis major in the axillary nodes and in larger nodes of the lateral thoracic and internal mammary chain. The mesial part of the breast drains into the internal mammary nodes and thence to the anterior mediastinal group. There are communications between the pectoral lymph channels of the two breasts accounting for "cancer en cuirasse."

The breast is essentially a mass of glandular tissue—a specialized skin organ. It is composed of a number of lobes, approximately twelve to sixteen, separated by layers of connective and adipose tissue. Each lobe is composed of small glandular structures with acini that secrete milk and is therefore an independent compound alveolar gland in itself. These empty into ductules which in turn empty into the four or five main ducts that widen into ampullae and then become narrow before emerging in the nipple. Each lobe is thus composed of lobules separated by dense connective tissue (interlobular) which contains much adipose tissue. The intralobular connective tissue is much more cellular than the interlobular and contains fewer collagenous fibers and practically no fat. The interlobular connective tissue carries vessels, nerves, and lymphatics. The area around the nipple is pigmented. It is equipped with special sebaceous glands (glands of Montgomery) that secrete an oily substance. The nipple is easily everted, due to erectile tissue, permitting the infant to nurse. The breast is intimately connected with the pituitary gland and ovaries in its physiological function. In a developmental way the breast changes at three stages of life. First, the change that occurs with the onset of menstruation. The breasts enlarge due to glandular development (evolutionary stage). Then, with pregnancy, the so-called lactation hormone is secreted, causing the breasts to enlarge and develop still further, and with the delivery of the baby (third or fourth day post partum), a profuse flow of milk occurs (functional stage). The third stage is at the menopause, when the glands lose their functioning ability and the epithelium of the acini and, to a lesser extent, the ducts undergo an involutionary change with atrophy, so that the breasts become saggy and devoid of structure, hanging like empty sacks with a small amount of atrophied glandular tissue

in their dependent portions. The interstitial connective tissue becomes less cellular and the collagenous fibrils decrease. The framework becomes a homogeneous, finely granular mass. These changes are normal and physiological.

The tubular mammary gland peculiar to mammals is a modified apocrine gland (see Chapter 22). The nature of such glands which occupy an intermediate position between holocrine and merocrine glands is that a part of the cell or its cytoplasm is extruded with functional activity. The nucleus is left intact and soon the cell recovers. Thus the mammary gland is related to certain sweat glands (q.v. Chapter 16) as shown by the myoepithelial cells which are prominent near the excretory ducts. Indeed certain epithelial tumors and cysts of the breast also show this close relationship. The most characteristic expression of the secretory function of the glandular cells are the drops of fat which accumulate in the end of the cell protruding into the lumen and which pass out of the protoplasm, leaving a defect in the cell which is soon repaired. Whether or not these cells secrete a small amount during each menstrual cycle is not definitely known. Some women with strong hormonal stimulation (estrone and progesterone) do have a primitive colostrum-like secretion with each cycle. The changes which occur with menstruation are probably due to hyperemia and some edema of the interstitial connective tissue. Some observers believe that there is a cyclic hyperplasia in the ductule and acinar epithelium with desquamation, very much as the endometrial changes in the uterus, and therefore the breast goes through a cycle of cellular proliferation and desquamation giving rise to pain, swelling, and nodularity in the breast before menstruation and also swellings of the axillary nodes which are thought to be due to the presence of phagocytosed desquamated cells and debris carried by the lymphatics.

Malformations of the Breast

Some persons are born with malformations of the breasts. Normal variations in the size and shape of the breast are found. Frequently one is larger than the other. *Virginal hypertrophy* means unusually large breasts in adolescent girls or nulliparous young women which may attain such size that they become bothersome and embarrassing. It may involve one or both breasts, usually both. The enlargement is due to hypertrophy of all elements but chiefly the connnective and adipose tissue. The cause is not known but is said to be due to excessive estrogenic hormone stimulation. Occasionally surgeons are called upon to remove part of the breast tissue, rarely to perform a complete mastectomy. *Athelia* is the absence of nipples; the occurrence is rare. It is not pathological and does not lead to disease. However, it does lead to complications when pregnancy and lactation occur, because the milk is formed in the breast and has no exit. Surgeons sometimes make an opening in the breast. Retracted or small nipples are troublesome anomalies in the lactating breast. *Micromazia* is incomplete development. It means that the breast has never undergone proper development and is therefore useless for nursing. *Amazia* is the absence of the entire breast. *Polythelia* or supernumerary nipples are sometimes found. It is an atavistic tendency on the part of nature and reminds one of a sow or dog. The nipples may or may not be connected with breast tissue. In the event of the former, milk may be secreted from four to six nipples if one is nursed. Sometimes when they are in the axilla they are a source of annoyance. We have seen one case

where the only source of milk was in the abnormal nipple in the axilla, and and another case of eight nipples, four of which secreted milk. *Polymazia* means supernumerary breasts or nipples. *Hyperthelia* means the presence of supernumerary nipples with only two breasts. *Gynecomazia* means overgrowth of the breasts in the male. It is embarrassing but not pathological. It does not mean that the person is a hermaphrodite. This is a popular but erroneous belief. It is often associated with small testes and aspermatogenesis and not infrequently with impaired hepatic function, malnutrition, and chronic ulcerative colitis.

FIG. 144.—Hypertrophy of the breasts in a woman aged 28 years. A plastic operation was performed.

DISEASES OF THE BREAST

Diseases of the breast may be divided into those occurring in women under 40 years of age and those in women over 40. This is an arbitrary age and is based upon a study of diseases which are seen usually, *but by no means invariably*, in the age groups mentioned. At all ages functional disturbances occur. Abnormal secretions from the nipple are discussed later. Pain or mastodynia is usually caused by the cyclic turgescence which precedes menstruation. Often there is no assignable cause, especially in extremely nervous women. The complaint deserves careful

investigation. We have found that often *a proper support for pendulous* breasts which must be fashioned to fit each breast is a great help. Otherwise aspirin and local heat is useful.

Breast Lesions Which Occur Under 40 Years of Age.—

Mastitis (nonspecific)
1. Mastitis neonatorum
2. Mastitis of mumps
3. Mastitis of puberty
4. Lactation mastitis
5. Chronic plasma cell mastitis
6. Chronic mastitis, chronic cell mastitis

Tuberculosis of the breast
Actinomycosis and blastomycosis
Injuries and wounds, fat necrosis, and foreign bodies
Single and *multiple tumors and cysts*

MASTITIS.—

Mastitis Neonatorum.—Mastitis neonatorum is an inflammation of the breasts in the newborn. It is usually brought about by injudicious care of the baby. Many infants show a slight swelling and have a slight secretion from the breasts (colostrum) (it has been called "witch's milk") on the fifth or sixth day. This is thought to be due to the influence of estrogenic and mammotropic hormones derived by placental transmission. Menses sometimes occur also. Uninformed and superstitious women are apt to squeeze or traumatize the infant's breast, causing *subsequent infection.*

Mastitis of Mumps.—Mastitis of mumps is an unusual complication which usually subsides without abscess formation.

Mastitis of Puberty.—Mastitis of puberty may be due *to trauma* or "caking" of the breast. The latter is due to coagulation of "colostrum," with subsequent injury, or, as in the case of lactation mastitis, "caking" may so lower local resistance that indigenous bacteria may become active. This occurs at the age of puberty in either sex. A good plan is the use of a soft pad for protection.

Lactation Mastitis.—Lactation mastitis is not uncommon. It has all of the signs and symptoms of an abscess (Chapter 5). Usually it occurs *in the first two to three weeks post partum. Some say* it is due to a fissure or crack in the nipple. Sometimes we see the condition ante partum. It is probably due to indigenous bacteria which grow because of a lowered local resistance instigated by "caking" *which traumatizes* the breast as any foreign body does. The "caking" in turn is due to an overabundance of milk. In recent experiments on dogs we found that breast tissue is much more susceptible to *Staphylococcus aureus* infection than the rest of the abdominal wall. There is swelling, excruciating pain, and the presence of a tender, hard lump in the breast. The patient has fever, malaise, and anorexia. The prevention of this painful complication of pregnancy consists of cleanliness, gentleness, and release of

milk pressure. Some advise boric acid wash for the baby's mouth and mother's nipple before each nursing. Others use ointments on the nipple on the theory that softening them prevents "cracking." It is perhaps better to use nothing at all or 70 per cent alcohol to "toughen" the nipple. When an inordinate supply of milk is present, gentle breast pumping is indicated to avoid caking. Should infection develop, it is best to wait until localization has occurred. Lactation may be stopped by the use of large doses of estrogen. Then radial incisions should be made similar to the spokes of a wheel. This is done to avoid cutting across the main ducts with subsequent fibroses and retention cyst formation.

Chronic Plasma Cell Mastitis.—Chronic plasma cell mastitis is rare. Because of its firmness and painlessness it is frequently diagnosed as carcinoma. It usually involves one breast. Mild signs of inflammation may be present and occasionally there is a watery or creamy discharge from the nipple. There is skin dimpling and nipple retraction with enlargement of the axillary nodes. The cause of the disease is unknown. It is thought to be due to extravasation of material from the ducts into the periductal tissue—essentially an irritation by fat of milk or colostrum. Other theories are that the lesion is due to fat necrosis caused by trauma, bacterial infection, or virus infection such as that seen in association with lymphopathia venereum. Decomposing fatty material is probably the exciting factor. Histologically the lesion may resemble fat necrosis in its later stages which is characterized by plasma cells, lymphocytes, giant cells, and epithelial hyperplasia. Fat necrosis thus may resemble the medullary type of adenocarcinoma. Plasma cell mastitis as seen histologically shows ulceration of normal epithelium of the ducts which is replaced with granulation tissue; for this reason it is also called mastitis obliterans; the formation of foreign body giant cells gives it the name pseudotuberculosis, and the periductal collections of plasma cells and other leucocytes give it the name plasma cell mastitis. Intraductal accumulations of colostrum, cells, and leucocytes may show the presence of an *associated diffuse comedomastitis resembling comedocarcinoma. The* gross lesion appears as a yellowish-brown discoloration of the mammary tissue often associated with abscess formation. Indeed a correct diag*nosis cannot be made without removing tissue for biopsy although it may* be strongly suspected, especially if there are many plasma cells in the circulating blood stream. The treatment is palliative and mild x-ray.

Chronic Mastitis, Chronic Cell Mastitis.—Chronic mastitis, chronic cell mastitis may resemble the plasma cell variety clinically but not microscopically. There is usually pain and axillary lymphadenopathy with a hard firm, mass occupying most of the breast. We have recently seen this in a young woman following radical mastectomy of the opposite breast for adenocarcinoma. The skin has the thickened pig-skin appearance; the cut section is white and firm with little fat and occasional cysts. Histologically there are small cysts of the acini and ducts and some hyper-

plasia of epithelium; the intralobular stroma is edematous with lymphocytic infiltration. The interlobular stroma shows lymphocytic infiltration also. Simple mastectomy may be necessary to make the diagnosis. If proved by biopsy, a breast support is all that is necessary.

TUBERCULOSIS OF THE BREAST.—Tuberculosis of the breast is also rare. The signs and symptoms are no different from those of tuberculosis elsewhere. The disease is secondary to tuberculosis elsewhere and usually asserts itself by a breast lump after pregnancy. There is lack of pain in the breasts. The axillary lymph glands are enlarged. Many draining sinuses arise. The treatment is directed against the general tuberculosis, of which this is secondary. In addition, mastectomy with axillary node excision is necessary. Often the ribs and cartilage are involved requiring their removal.

ACTINOMYCOSIS AND BLASTOMYCOSIS.—Actinomycosis and blastomycosis have been encountered in our clinic. The chronic draining sinuses, surrounded by scarred and indurated tissues, suggests the diagnosis, which is established by smears and tissue from biopsy. The lymph glands are not involved.

In early localized infections, mastectomy may effect a cure. Later, iodides are used internally and x-ray treatment locally.

INJURIES, WOUNDS, FAT NECROSIS, AND FOREIGN BODIES.—Almost every woman with a lump in her breast gives a history of some injury. Usually the blow was unnoticed until months or years later. It is very difficult to attach much significance to such stories. *Traumatic* fat necrosis may result from such contusions. While in themselves harmless the resulting nodule may resemble carcinoma clinically and biopsy may be necessary to make the proper diagnosis. Simple excision hematomas, wounds with milk fistulas, and foreign bodies, present no real difficulties in diagnosis or treatment. However, when in doubt biopsies should be done in addition to the routine care of such wounds.

Single and Multiple Tumors and Cysts.—In a woman under 40 years of age a single hard lump is probably a fibroadenoma. If the connective tissue elements predominate, it is known as an adenofibroma. These rarely become malignant, giving rise to low-grade carcinoma or sarcoma. Lewis has called attention to the relationship between fibroadenoma and granulosa-cell tumor of the ovary. This may be due to the hormonal stimulation of the breast but the modus operandi is not clear. If it is a single soft mass, it is probably a retention cyst, or galactocele. It is painless and *freely movable* in the tissues. The single hard tumor is solid and is composed of adult fibrous tissue and many normal glands, surrounded by a capsule. Therefore it is not fixed to adjacent tissues. A cyst transmits light and is softer than the solid tumors. It is an epithelial wall filled with straw-colored fluid or milk (galactocele). Multiple tumors are usually intracanalicular fibromyxomas. They are hard, freely movable and slightly painful, and are usually seen in young girls. These new

growths and cysts should be removed. A general anesthetic should be used, the growth or cyst, with the capsule, should be removed and then always submitted to the pathologist for microscopic examination. Multiple painful cysts which feel hard are sometimes found in young women; usually women with scanty menses and small breasts who are between 30-40 years and are nulliparous. If there is no bloody discharge from the nipple estrogenic hormone may give relief although the carcinogenic potentialities of estrogen in "susceptible breast must be borne in mind, even when given in small doses. For a continuation of this discussion see chronic cystic mastitis.

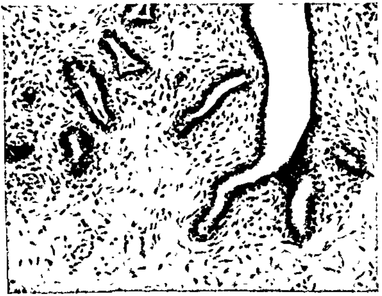

Fig. 145.—Pericanalicular fibromyxoma. The tumor was about the size of a small orange. It was removed from the breast of a girl aged 12 years. The connective tissue about the smaller ducts and canaliculi is involved.

Other benign tumors are simple encapsulated fibroma, encapsulated cystadenoma which is like a fibroadenoma except that the ducts are dilated into many small cysts, and lipoma. The nonencapsulated benign tumors are the pericanalicular fibromas which are probably more of a diffuse fibrous proliferation without duct destruction rather than new growths. They are seen commonly in the male breast. Benign duct papillomas which are small and do not cause cysts are important because they frequently cause bleeding from the nipple, q.v. Probing the ducts has been practiced so that the affected duct may be identified. This method is unsatisfactory as a rule because it often fails; the trauma induced by the probe is painful and may also cause bleeding. Any material obtained by the probe should be stained for cells. If no palpable tumor is present, a simple mastectomy may be necessary to rule out intraductal carcinoma. Warren has used the term adenocystoma to denote true intraductal papillary growths, commonly in the ampulla or larger ducts. It does not include the papillary projections of chronic

Fig. 146.—Intracanalicular fibromyxoma of the breast. The slitlike, epithelium-lined areas are the walls of invaginated canaliculi pushed inward by the tumor.

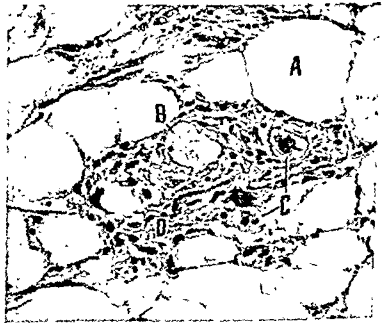

Fig. 147.—Fat necrosis in the breast. Medium-power photomicrograph showing the early changes in fat necrosis. This shows a clump of degenerating fat globules with fibrous tissue and phygocytic reaction. *A.* Unaffected fat globule. *B.* Degenerating fat globule. *C.* Giant cells. *D.* Young connective tissue cells. This lesion may resemble carcinoma clinically because it is a single tumor mass which is fixed in the tissues and is hard.

cystic mastitis. Adenocystoma is definitely a precancerous lesion. A rare type of cystic disease of the breast is due to apocrine type glands which become dilated and form multiple apocrine cysts or "butter cysts," so-called because of their contents which are thick and at times malodorous; also the term hidradenocystoma has been used. They are important because occasionally carcinoma arises in them. They should be removed. Microscopic studies show the cysts to be lined with apocrine type of epithelium. These cells have been called hidradenocytes and the term hidradenoma used to describe benign intraductal papilloma or papillomas in cysts containing these cells. Axillary apocrine glands as well as those which may be present in the breast adventitiously may undergo enlargement with each menstruation. *Malignant tumors* in young women are not rare. In the "under 40" group may be listed carcinoma which may be of the acute "inflammatory" type or sarcoma, usually fibrosarcoma, and rarely periductile myxoma or myosarcoma (cystic sarcoma, adenosarcoma), a cellular growth with much edema, hemorrhage, cyst formation, and necrosis. Radical excision of the breast and surrounding tissues, including all anatomical nodes, is the treatment of choice. In sarcoma, an x-ray study of the lungs and bones must be made first. If no metastases are present, radical surgery is necessary to effectuate a cure and this must be done early. A more complete discussion of malignant disease of the breast follows later in this chapter.

Breast Lesions Common After 40 Years of Age.—

- Plasma cell mastitis
- Tuberculosis
- Fungus infections
- New growths
  - Multiple tumors
  - Single tumor

PLASMA CELL MASTITIS.—Plasma-cell mastitis which has been described occurs in all age groups.

TUBERCULOSIS AND FUNGUS INFECTIONS.—Tuberculosis and fungus infections are not uncommon. These have been described in Chapters 7 and 8.

NEW GROWTHS, CHRONIC CYSTIC MASTITIS.—Far more frequent are new growths. These may be multiple. As we have seen in Chapter 15, multiple growths are usually benign. In addition, they may be painful. However, some women under 40 with every menstrual period have pain and small masses in their breasts which soon disappear. These are usually women who are unmarried and have scanty menses. In older women this same phenomenon is observed but the tender lumps persist. This condition has been called *chronic cystic mastitis,* although it is not a mastitis and is not always cystic. The entire problem is intimately related to hormonal imbalance or other constitutional agents as yet unknown. Perhaps local vascular factors play a role. The importance of the breast

changes which are grouped under this heading is their relation to carcinoma which is more than coincidental. We have noted that with each menstrual cycle there is stimulation and regression. This is shown histologically by hyperplasia of the periductal connective tissue and the epithelium (to a less extent) of the ducts which grow if pregnancy occurs. There is also increased vascularity with the estrus cycle. All of this is related to the ovarian hormones (estrogen, progesterone), the anterior pituitary hormones (galactogogue), adrenal-cortical hormone, and the testicular or androgenic hormones in the male. The exact relation-

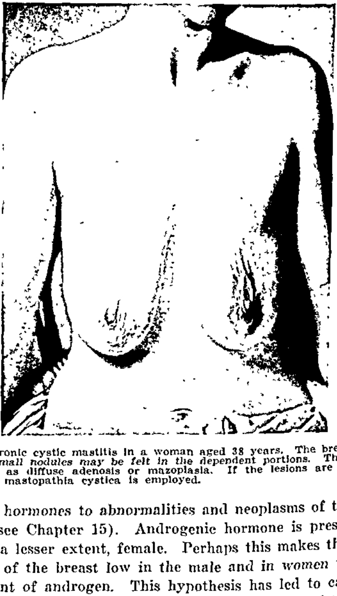

Fig. 148.—Chronic cystic mastitis in a woman aged 38 years. The breasts hang like empty sacks. Small nodules may be felt in the dependent portions. This condition is also referred to as diffuse adenosis or mazoplasia. If the lesions are predominantly cystic, the term mastopathia cystica is employed.

ship of these hormones to abnormalities and neoplasms of the breast is not known (see Chapter 15). Androgenic hormone is present in both male and, to a lesser extent, female. Perhaps this makes the incidence of carcinoma of the breast low in the male and in women who have a greater amount of androgen. This hypothesis has led to castration in the female with carcinoma of the breast and to the use of testosterone. There is no proof, however, that such is the case in the human being. During adolescence, chiefly because of estrogenic stimulation, the breast enlarges not only because of its connective tissue framework but also

because of its epithelial (glandular and ductal) elements. The menopause brings loss of weight generally and especially in the breasts. Interlobular fat disappears, the acini shrink, and their epithelial lining is practically desquamated. Nothing remains but dilated ducts, some periductal connective tissue, and an atrophic skeleton. This involutional change may give rise to functional aberrations and organic changes. The former may be manifested by pain and serous or milky or bloody discharge (which is practically always due to a papilloma and not vicarious menstruation) from the nipple. The organic changes may in-

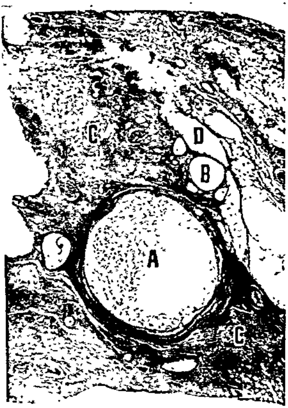

Fig. 149—Apocrine cysts of breast. Summar photograph (×10-75 diameters without use of microscope) of the breast with multiple apocrine cysts (butter cysts). *A.* Cyst. *B.* Smaller cyst with definite apocrine lining. *C.* Connective tissue. *D.* Flattened apocrine cyst with atrophic lining.

volve any or all of the breast elements. (1) The involutional process causes a reaction in the breast and soon the acini are surrounded by fibrous tissue which may proliferate in great abundance, completely enclosing or displacing the acini, which become involved in small fibrous scars, adenofibrosis. (2) Hyperplasia of glandular and ductal elements. Sometimes the hyperplasia is not regular, with variation in size and shape and staining reactions of the cells. This is more or less a precancerous lesion although there is no breaking through of the basement mem-

brane. If the hyperplasia involves mostly acini, the term adenosis or diffuse adenosis is applied and is comparable to adenosis of the thyroid gland. Small cystic areas may be present. This gives rise to the so-called "shotty" or "lumpy" breast and is known as *mazoplasia*, adenosis, sclerosing adenomatosis, or the *maladie cystic* of Reclus. (3) If the ductules are occluded partially and the acini incompletely, they are stimulated to secrete a primitive fluid, giving rise to many small cysts (blue-domed cysts of Bloodgood). This is known as the *cystiferous* breast or *mastopathia cystica*. Chronic cystic mastitis is usually seen in women with small or incompletely developed mammary glands. It is more common in those who have not borne children or who have had a relatively long period of sterility. In other words, women who bear children regularly develop a sort of immunity to the evolutionary and

Fig. 150.—Chronic cystic mastitis (cystiferous breast). Medium-power photomicrograph of a nodule in chronic cystic mastitis or Schimmelbusch's disease. *A*. Small cyst with hypertrophic lining. *B*. Connective tissue. *C*. Proliferating secretory epithelium. (16 mm., low power, 8 mm., medium power; 4 mm., high power dry; and 2 mm. high power oil.)

involuntary changes that occur with each pregnancy, so that fibrous tissue and epithelial reactions and epithelial desquamation are minimized when the menopause occurs. This is probably due to a control of the local resistance of the breast due to increased blood supply and functional activity initiated by the lactating and other hormones.

The diagnosis rests on the fact that there are multiple tumors, in both breasts, as a rule, which are freely movable and feel like a "bag of peanuts" and there is pain and tenderness in both breasts. It is difficult to distinguish between the cystiferous, the adenofibrotic, or the mazoplastic breast (often the three types occur simultaneously), but the breasts with epithelial hyperplasia (mazoplasia or adenosis) are more painful and more apt to be precancerous. However, the cystic type is

also dangerous because of the possibility of papillomatous growths within the cyst which may cause a bloody discharge from the nipple and not infrequently result in carcinoma. The percentage of carcinoma is said to be greater in a breast with chronic cystic mastitis than in the normal; therefore, the physician must be wary of any lumps. For this reason he prepares a chart for his patient. If he discovers anything unusual, he will note its size and position on the chart. In a month he will see the patient again. If the lesion is a chronic mastitis, the tumors will change in size and position. If a growth remains unchanged and has increased in size he will remove it for microscopic study. A liberal section of breast tissue which includes the nodule should be removed. If the microscopic features are those of epithelial hyperplasia with questionable neoplastic cells, then a simple mastectomy is indicated. Warren found that the breast cancer rate for women with chronic cystic mastitis and related lesions in the age group from 30 to 49 years is 11.7 times the rate for the Massachusetts normal female population; in the group over 50 years of age, 2.5 times as great; and the entire group 4.5 times as great. During the observation period before biopsies are deemed necessary local heat and anodynes may be given to relieve pain. *Estrogens are not indicated because they may incite epithelial proliferation and breast engorgement.* The androgens and progesterone may result in temporary improvement. Abolition of ovarian function by x-ray or surgical removal of the ovaries, though not advised by us, does relieve pain and sometimes causes a disappearance of nodularity.

Abnormal Discharge From the Nipple

Abnormal discharge from the nipple may be extremely varied. We have observed the following types: watery, milky, purulent, serous, serosangineous, bloody, and combinations of these. Watery discharge from the nipple is of no great importance. It is seen at all ages from adolescence to the menopause and is probably due to excessive hormonal stimulation. It may be artificially induced by stilbestrol or estrogenic hormone therapy. Milky discharge is not uncommon in infancy (colostrum), adolescence, before and after the lactation period in pregnancy, and associated with chronic mastitis. This galactorrhea is due to the early stages of lactation and is associated with hyperplasia of the acini. Later the ducts become filled with desquamated cells and stagnating secretion. Periductal inflammation, cysts, and hyperplasia of duct epithelium may follow. Purulent discharge is associated with lactation mastitis, plasma cell mastitis, rarely, tuberculosis, and fungus infections of the breast. Yellow serous discharge is observed in chronic cystic mastitis of any type, fat necrosis, or tuberculosis but may also be associated with functional derangements or benign intraductal papilloma. Serosanguineous or bloody discharge from the nipple is ominous. It is found in Paget's disease, intraductal papilloma, benign or malignant, proliferative papillary cystadenoma, adenocystoma, and all types of carcinoma

but chiefly in intraductal or cystadenocarcinoma and hemangioma. *A bloody discharge from the nipple demands surgical exploration.* It is almost always associated with an intraductal papilloma or carcinoma. The differential diagnosis can be made only by microscopic examination. Frequently there is no palpable breast tumor or lymph nodes in the axilla and yet extensive diffuse carcinoma may be present. It is our custom to do a simple mastectomy—the breast is quickly sliced and the slices placed on a long board. Each slice is inspected carefully and all suspicious lesions are cut out for frozen section. Should the lesions

Fig. 151.—Intracystic papilloma of breast. Medium-power photomicrograph of an intracystic papilloma. *A.* Fat. *B.* Wall of cyst. *C.* Remaining lumen. *D.* Papilloma. It is this type of lesion that may give rise to bleeding from the nipple. The lesion is serious because of its tendency to become carcinomatous.

be benign, no further surgery is done. If malignant, radical mastectomy is performed. Later the breast is hardened in formalin and cut with a meat slicer into thinner sections and the process of gross and microscopic section is repeated. By this routine we have found that (1) occasionally a small carcinoma has been overlooked and subsequent radical surgery was necessary; (2) when a palpable tumor has been biopsied or when several tumors have been removed for histological study an incorrect report of chronic cystic mastitis or adenosis has been made; then subsequent simple mastectomy done for persistent serosangineous discharge from the nipple has revealed early adenocarcinoma.

Carcinoma of the Breast

Etiology.—The cause of carcinoma is unknown. Recent experimental work has been summarized in Chapter 15. Some pertinent observations that are no doubt related to breast cancer should be reviewed.

Trauma.—Almost every woman with a lump in her breast attributes the lesion to an injury. There is no clinical or experimental proof that a single injury may cause carcinoma. However, *fat necrosis* may closely simulate carcinoma clinically and even microscopically. There may be a relationship to carcinoma in this way. Therefore the single, slightly painful hard lump should be removed for careful microscopic study.

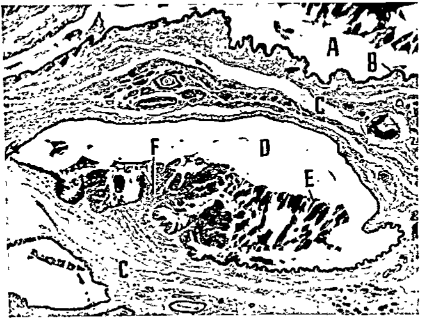

Fig. 152.—Intraductal papilloma of the breast. Low-power photomicrograph of an intraductal papilloma. *A.* Adjacent normal duct. *B.* Normal lining of duct. *C.* Connective tissue. *D.* Duct containing papilloma. *E.* Blood clot. *F.* Papilloma. This lesion is apt to give rise to carcinoma of the ductal variety (comedocarcinoma). Clinically it manifests itself by bleeding from the nipple. Bleeding is more apt to occur from an intraductal papilloma than from an intracystic papilloma because the latter would of necessity have to have communication with a duct in order for the blood to exude from the nipple.

Age.—No age is immune; the decade 50 to 60 years shows the largest number, with 40 to 50 years next. Although there are many studies to the contrary, our observations show a greater virulence of carcinoma in the young than in the old. In fact, the disease is not the same in its rapidity of growth, tendency to metastasize, and response to treatment in those over 70 years. Inflammatory carcinoma seen in the young is a deadly disease not amenable to any known therapy. Carcinoma after 70 years is slow and with the "strongly resisting" lymphatics the disease tends to remain local. Recurrences are not uncommon but they are usually accessible and may be removed. It is best to regard the disease as

deadly and equally amenable to treatment at all ages and to apply the *same radical treatment whenever the disease is encountered* if the patient can stand it.

Heredity.—Heredity plays a role. In 20 to 30 per cent of cases of mammary cancer there is probably an inherited susceptibility and in the female relatives of these women the incidence of breast cancer is said to be 3 times greater than in the general population. (See Chapter 15).

Fertility.—Carcinoma of the breast is seen more in women who have borne children because approximately two-thirds of the white women in this country bear children. However, *nulliparae are more prone* to develop cancer than those bearing children. The prognosis is the same in both groups.

Fig. 153.—Sclerosing adenomatosis of the breast (Summar photograph). *A.* Mass of adenomatous proliferation of the secretory acini *B.* Group of dilated ducts. *C.* An area of adipose tissue. This lesion is often mistaken for carcinoma, although it is benign and well localized as a rule. Actually it does not resemble carcinoma in all cases. However, if there has been much fibrosis, it may resemble carcinoma.

Lactation.—All experimental and clinical observation lends support to the belief that failure of the breast to perform its physiological function properly is the *most consistent apparent factor* in the genesis of cancer. The practice of "drying up the breast" and feeding the baby from the bottle is a deplorable fad which is a burden on the baby and a menace to the mother. We have recently operated upon a woman 49 years old with cancer of the breast who has borne fourteen children but she did not nurse any of them.

Estrogens *and the pituitary hormones are necessary* for the development of the mammary gland. Cancer occurs practically always in a breast that has undergone a certain degree of development. Presumably the estrogenic hormones produce an anatomical development sufficient to

allow the cancer process to manifest itself. Do estrogens act as carcinogenic agents? (1) In cancer strain mice the incidence of mammary cancer can be reduced to almost zero if the ovaries are extirpated in the very young (except the newborn)—this must be done before sexual maturity and the younger, the lower the incidence. (2) Cancer of the breast does not occur in male mice of a high cancer strain spontaneously. It does occur after the injection of large quantities of estrogen continued over long periods. Therefore, cancer of the breast in male mice of high cancer strain does not develop spontaneously because the hormone necessary for stimulation of the mammary gland is not present. (3) Diethylstilbestrol given to mice in (2) develop cancer. Therefore it is not the chemical per se but its effect physiologically that induces cancer; furthermore, cancer does not occur at the site of injection. (4) Incidence

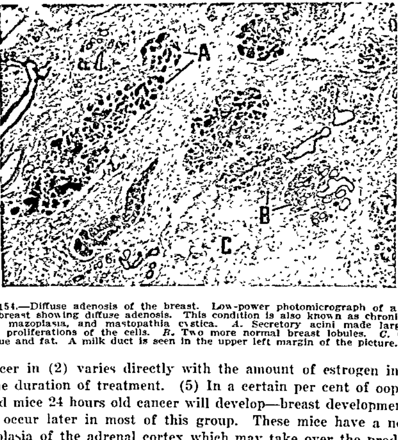

Fig. 154.—Diffuse adenosis of the breast. Low-power photomicrograph of a section from a breast showing diffuse adenosis. This condition is also known as chronic cystic mastitis, mazoplasia, and mastopathia cystica. *A*. Secretory acini made larger and solid by proliferations of the cells. *B*. Two more normal breast lobules. *C*. Connective tissue and fat. A milk duct is seen in the upper left margin of the picture.

of cancer in (2) varies directly with the amount of estrogen injected and the duration of treatment. (5) In a certain per cent of oophorectomized mice 24 hours old cancer will develop—breast development and estrus occur later in most of this group. These mice have a nodular hyperplasia of the adrenal cortex which may take over the production of estrogen. (6) Besides estrogenic stimulation, the "milk factor" (see Chapter 15) may play a role. (7) *Many clinical reports of cancer of the breast thought to be due to estrogenic therapy have been reported—none proved.* (8) We have observed many men with carcinoma of the prostate who have received enormous doses of diethylstilbestrol. The breasts become greatly enlarged. We have not seen any cases of carcinoma

of the breast nor have we found any such reports in the literature. Most of these men are in the "proper" age group. (9) In most women with cancer of the breast menopause has occurred. The luteal hormone is absent but not the follicular; therefore, estrogenic stimulation is *decreased.* Here the explanation has been a loss of ovarian control over normal growth and stability of tissue in the breast allowing other unknown substances with growth-stimulating properties to act. (10 Estrogenic stimulation has not produced mammary carcinoma in rabbits or monkeys. (11) Testosterone or progesterone administered at the same time that estrogen is given to susceptible mice does not prevent cancer from forming. (12) The essential feature of estrogenic cancer is the acceleration or the prolongation of the ripening and maturity in the

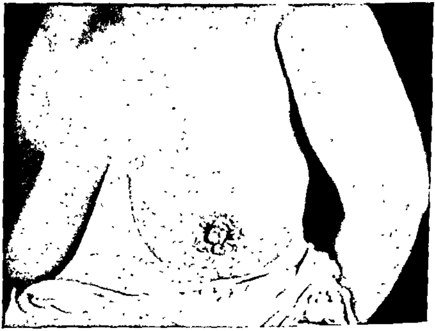

Fig. 155.—Large adenocarcinoma of the breast in a woman aged 48 years, with metastasis in the axillary glands but none in bones or lungs. The case was treated by pre- and postoperative x-ray therapy and radical resection.

mammary gland beyond physiological limits in mice. (13) Human mammary cancer may result from abnormally intense estrogenic stimulation during the adolescent period of mammary development or during a previous pregnancy; ovarian dysfunction in cyclic women resulting in relative hyperestrogenism over a period of years prior to the menopause (most of these have adenosis or cystiferous breasts); intense or continuous estrogenic stimulation at the time of the menopause (superimposed on the previous factors).

Summary: Experimental evidence shows a strong relationship between estrogenic stimulation and carcinoma of the breast, particularly in cancer strain mice. Estrogens in the human will cause an enlargement of the breasts when given in very large doses over a long period of time. The enlargement is due chiefly to an increased vascularity and

hyperplasia and hypertrophy of the connective tissue and, to a less extent, of the epithelial elements. Therefore there is a stimulation to growth of normal as well as to abnormal cells. As yet there is no definite proof that normal cells may be changed to cancer cells by estrogens in the *human being*—*estrogen therapy should be used cautiously* and if any breast abnormality exists it is perhaps better not to use the drug.

Pathology.—Various types of carcinoma occur in the breast. Adenocarcinoma is a mild form and more nearly resembles glandular architecture; medullary carcinoma, encephaloid carcinoma, and carcinoma simplex are soft cellular growths undergoing early necrosis; scirrhus carcinoma *is hard and fibrous, actually decreasing the size of the breast* (if the glands are involved they are small and hard); mucoid carcinoma shows a primitive secretion or mucoid degeneration; Paget's disease of the nipple may be a malignant dermatitis or duct carcinoma; a rapidly fatal variety is the acute inflammatory carcinoma of pregnancy. Duct cancer may occur at the beginning of the ducts (Paget's), at their termination, or along *their course (comedocarcinoma).*

Fig. 156.—Adenocarcinoma of the breast (medullary cancer). Note the scarcity of blood vessels, the small amount of stroma, and the variety of large malignant cells.

Ewing divides carcinoma of the breast based on anatomical features into (1) adenocarcinoma arising chiefly in cysts of ducts or sweat glands (apocrine); (2) duct carcinoma from the lining cells of ducts; (3) acinar carcinoma from the epithelium of the acini. *Subdivisions of these main* groups are mucoid carcinoma, fibrocarcinoma, and carcinosarcoma.

Paget's disease of the breast and of the vulva are similar. The resemblance to gland tissue has led to the opinion that the growths originate in the apocrine glands in the areola. Similar types of carcinoma have

of the breast nor have we found any such reports in the literature. Most of these men are in the "proper" age group. (9) In most women with cancer of the breast menopause has occurred. The luteal hormone is absent but not the follicular; therefore, estrogenic stimulation is *decreased*. Here the explanation has been a loss of ovarian control over normal growth and stability of tissue in the breast allowing other unknown substances with growth-stimulating properties to act. (10 Estrogenic stimulation has not produced mammary carcinoma in rabbits or monkeys. (11) Testosterone or progesterone administered at the same time that estrogen is given to susceptible mice does not prevent cancer from forming. (12) The essential feature of estrogenic cancer is the acceleration or the prolongation of the ripening and maturity in the

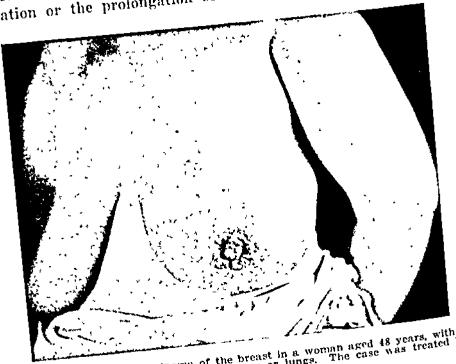

Fig. 155.—Large adenocarcinoma of the breast in a woman aged 48 years, with metastasis in the axillary glands but none in bones or lungs. The case was treated by pre- and postoperative x-ray therapy and radical resection.

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ivides carcinoma of the breast based on anatomical features ıocarcinoma arising chiefly in cysts of ducts or sweat glands 2) duct carcinoma from the lining cells of ducts; (3) acinar om the epithelium of the acini. Subdivisions of these main ıucoid carcinoma, fibrocarcinoma, and carcinosarcoma.

lisease of the breast and of the vulva are similar. The re- gland tissue has led to the opinion that the growths originate ine glands in the areola. Similar types of carcinoma have

of the breast nor have we found any such reports in the literature. Most of these men are in the "proper" age group. (9) In most women with cancer of the breast menopause has occurred. The luteal hormone is absent but not the follicular; therefore, estrogenic stimulation is *decreased*. Here the explanation has been a loss of ovarian control over normal growth and stability of tissue in the breast allowing other unknown substances with growth-stimulating properties to act. (10 Estrogenic stimulation has not produced mammary carcinoma in rabbits or monkeys. (11) Testosterone or progesterone administered at the same time that estrogen is given to susceptible mice does not prevent cancer from forming. (12) The essential feature of estrogenic cancer is the acceleration or the prolongation of the ripening and maturity in the

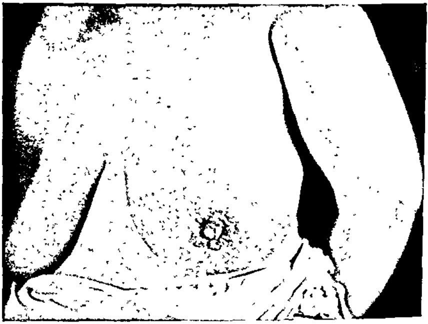

Fig. 155.—Large adenocarcinoma of the breast in a woman aged 48 years, with metastasis in the axillary glands but none in bones or lungs. The case was treated by pre- and postoperative x-ray therapy and radical resection.

mammary gland beyond physiological limits in mice. (13) Human mammary cancer may result from abnormally intense estrogenic stimulation during the adolescent period of mammary development or during a previous pregnancy; ovarian dysfunction in cyclic women resulting in relative hyperestrogenism over a period of years prior to the menopause (most of these have adenosis or cystiferous breasts); intense or continuous estrogenic stimulation at the time of the menopause (superimposed on the previous factors).

Summary: Experimental evidence shows a strong relationship between estrogenic stimulation and carcinoma of the breast, particularly in cancer strain mice. Estrogens in the human will cause an enlargement of the breasts when given in very large doses over a long period of time. The enlargement is due chiefly to an increased vascularity and

largest single lymphatic plexus in the body, the disease has access to all the parietal tissue, accounting for the wide dissemination of skin nodules in some late cases of cancer of the breast.

Since centrifugal permeation of the fascial plexus has been proved, this process must also carry cancer cells to the periosteal lymphatics of the subcutaneous areas, where the fascia is attached directly to the bone. As lymphatics and veins always run along together, infiltration of the wall of the concomitant vein is a likely event, and subsequent extension to the bone may take place along the blood channels. The involvement of the femur on the same side as the cancerous breast before the opposite femur is involved is a result of this process. Cancer of the breast may spread:

1. By *infiltration* through tissue spaces surrounding the primary focus, with the production of a lump. This is a slow and limited process.
2. By *permeation* of small lymphatic vessels of the deep fascial plexus.
3. By *lymphatic embolism* to the axillary glands, first of the same side, and later of the opposite side.
4. By *blood embolism*, a rare but positive event.
5. By *finding a portal of entry to the great cavities of the body as in para-sternal* invasion of the thorax.

Fig 158.—Paget's disease of the nipple. The low power shows the downward growth of epithelial cells through the skin and subcutaneous tissue, and their invasion of a duct. The high power shows the large malignant Paget cells, which are characteristic of this lesion.

An unrecognized law of cancerous growth:

Every aggregation of carcinoma cells has a definite life cycle, and, after increasing in size for a varying period and at a varying rate, tends spontaneously to undergo degenerative and fibrotic changes. These changes extend from the center of the mass centrifugally to its periphery, lead to shrinkage, and *terminate in the replacement* of the aggregation of cancer cells by a fibrous scar.

A permeated lymphatic undergoes a series of changes due to its distention and rupture by cancer cells which fill it and to the inflammatory process that reults. In the end the original lymphatic is replaced by a solid thread of fibrous tissue from which

been reported in the axilla and around the anus—common sites for apocrine glands. Paget cells may be malignant apocrine gland cells. Other sites of origin may be as follows: (1) the ductal epithelium extending up the ducts and permeating the lymphatics draining the nipple. The lesion advances by intraepithelial growth to the nipple involving it and later neighboring ducts and connective tissue. The cells infiltrate centrifugally from a single primary source and are malignant from the beginning; (2) it is derived from stratified squamous epithelium. Although there is some dispute concerning its origin, many factors seem to point to its apocrine gland origin. The important fact is that the disease is not an "eczema" or dermatitis but it is a malignant disease of the breast requiring radical surgery. Eczemas do occur in both breasts in young persons; Paget's disease is practically always seen in one breast. Biopsy may be necessary to make the diagnosis.

Fig. 157.—Paget's disease of the nipple in a woman aged 40 years. Radical resection was performed.

Perhaps more important than the varieties of carcinoma is the method of its spread:

Handley's Hypothesis.—Repeated observations have proved that the first local spread of the carcinoma takes place by a rapid process termed "permeation" which consists of the growth of plugs of cancer cells along the lymphatic vessels of the breast rather than by the slow process of infiltration. Permeation equal in all directions is the "master process" of dissemination, for it penetrates small anastomotic lymphatics where the stream is too sluggish and the vessels too narrow for the passage of emboli of cancer cells.

As a result of the rich network of intramammary lymphatics and its numerous communications with other parts of the lymphatic system, the disease is able to pass early and easily to parts beyond the breast. Many of these lymphatics run directly back to the fascial plexus overlying the pectoralis major muscle. Since this is the

and the subserous fat, and the linea alba is penetrated by lymphatic vessels. Because it is possible to guard against invasion by this route by removing the "dangerous" portion of the anterior layer of the rectus sheath, abdominal recurrence has become relatively rare in recent years.

Other factors explained on Handley's hypothesis are: carcinoma of the breast rarely permeates below elbow or knee. For if equidistant on all sides, it would involve vital structures in the thorax and elsewhere, causing death.

The most common bone site is in the humerus, where the deltoid muscle is inserted, and the greater trochanter of the femur—the deep fascia is closest to the bones at these sites.

The vetebrae are involved by permeation along intercostal lymphatics involving dorsal nerve roots long before the vertebrae themselves are involved. This explains the severe pain before x-ray evidence of metastasis.

Permeation is equidistant in all directions. This explains the bad prognosis when axillary glands are involved. Mediastinal glands may also be involved.

Permeation is along the deep tubular lymphatics first. Along the deep fascia, then, there is retrograde involvement of the reticular lymphatics. The perilymphatic fibrosis set up by the cancer cells causes lymphatic obliteration which interferes with lymph drainage, producing edema late (cancer en cuirasse) or pigskin appearance early. It is unfortunate that there is permeation first, then fibrosis, rather than the reverse.

Metastasis may reach the abdomen by way of the rectus sheath (or deep fascia) up the ligamentum teres or falciform ligament of the liver, and into the porta hepatis, and then break through the liver capsule.

Carcinoma penetrates the chest wall and involves the pleura first, then the lungs.

Theoretically, all of the local cancer area can be removed. This may not prevent the growth in distant areas already permeated but does prevent any local recurrence.

Symptoms and Signs.—A single growth in one breast in a woman past 40 years old is carcinoma until proved otherwise. The classical symptoms and signs are

1. A single growth in one breast.
2. The growth is *painless.* Pain occurs only in *late* carcinoma.
3. It is fixed to the skin or surrounding tissue. This is elicited by moving the growth gently in a circular manner producing a slight tug on the skin.
4. Some retraction of the nipple (if the growth is near it).
5. A pigskin appearance over the growth due to blockage of the connecting lymphatics in the ligaments of Cooper.

These are the early symptoms and signs. Later there is large growth with fixation of the entire breast, enlargement of the axillary glands, *local ulceration, edema of one* or both breasts (cancer en cuirasse), pain in the breast (nerve invasion) and back (vertebral metastasis), extreme loss of weight, cachexia, metastasis to the lungs and liver, and ultimately death.

Prognosis.—From questionnaires sent to patients who had been operated upon for carcinoma of the breast in the Indiana University Hospitals, we may state that in all cases (early and late) our five-year cure is about 33 per cent; the *early ones, about* 67 per cent. However, a five-year cure does not mean a cure. It means the disease has been arrested for five years. Fifteen- or twenty-year cures would really reveal *cures.*

cancer cells have disappeared. This process has been named perilymphatic fibrosis. Thus, the carcinoma apparently heals in its central portions while spreading at its periphery.

Parasternal Invasion of the Thorax.—Simultaneous with invasion of the axillary glands there is an invasion of the glands of the internal mammary chain which lie behind the costal cartilages lateral to the sternal border. These glands do not lie in the range of operation and there are no clinical methods by which their condition can be determined. The failure of a well-planned operation for breast cancer is now most frequently explained by the unsuspected early invasion of the parasternal glands. (This usually manifests itself after a period of about three years but may not appear for as long as fourteen.) A study of scientifically planned operations has revealed "local and axillary recurrences to be reduced almost to zero and more than half the recurrences are found either as nodules at the inner ends of the upper intercostal spaces, or show themselves in the supraclavicular triangle, the glands of which are connected with the internal mammary chain." (Handley.)

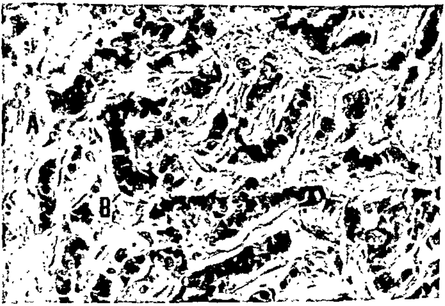

Fig. 159.—Scirrhus type carcinoma of breast.—Photomicrograph of scirrhus carcinoma of the breast. This might also be termed, a scirrhus type of carcinoma simplex with rows of cancer cells separated by connective tissue. This is the type that, as time goes on, becomes more and more filled with connective tissue and then the cancer cells become atrophic. In fact, the entire lesion becomes smaller so that it has been aptly said that this is one type of carcinoma of the breast in which, as it grows, the breast becomes smaller. Finally, the picture is one of scar tissue with a few cancer cells remaining in it. *A.* Connective tissue between the masses of cancer cells *B.* Linear arranged carcinoma cells.

The patient begins to complain of pain along the edge of the sternum on the side of the operation. Small nodules soon appear at the inner ends of the upper intercostal spaces. The skin becomes adherent to the nodules and ulceration follows. The tumor in the superior mediastinum causes dyspnea and dysphagia due to pressure on the trachea and bronchi and pressure on the recurrent laryngeal nerve and the esophagus. Pleural effusion and cardiac failure may supervene as terminal events. Autopsy shows a mass of growth filling the superior and anterior mediastinum and infiltrating the sternum.

Epigastric Invasion of the Abdomen.—The lower and inner margin of the breast reaches to within an inch of the ensiform cartilage, a region in which the body cavity is poorly defended against the attack of permeation. At the tip of the ensiform the linea alba is the only layer intervening between the permeated fascial lymphatic plexus

and the subserous fat, and the linea alba is penetrated by lymphatic vessels. Because it is possible to guard against invasion by this route by removing the "dangerous" portion of the anterior layer of the rectus sheath, abdominal recurrence has become relatively rare in recent years.

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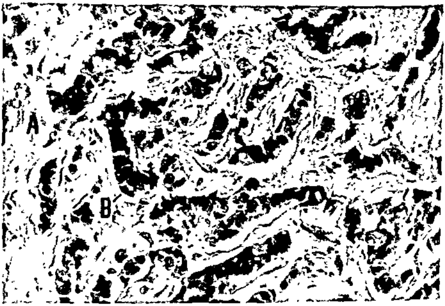

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of five years in Stage A are probably cured. Those in Stage C are apt to have late recurrences. Five-year cure should not be called a cure because *even in Stage A there may be ten-year recurrences* in 25 to 30 per cent.

The time elapsed since the onset is difficult to evaluate. Patients really do not know exactly when the lump began—they do know when they first discovered it. Therefore no patient should be refused surgery because of time or stage except in Stage E if the patient is in condition to stand radical surgery.

The prognosis of "inflammatory" carcinoma or cancer of the breast *occurring in gravid and puerperal women, "acute carcinosis,"* is extremely grave—we have not had a five-year cure by any method of treatment. Inflammatory cancer begins deep in the breast, spreads rapidly by the intramammary lymphatics, and is *usually well developed before it* is discovered. The inflammatory reaction is greater because the deep blood supply is prodigious. Mucoid carcinoma is less malignant as a rule than other types. Perhaps this is due to the fact that at least in some of these the mucin represents a primitive secretion showing a cell with some function and therefore a neoplasm which is less malignant.

It takes two to make the bargain in carcinoma—the "virulence" of the growth and the "resistance" of the patient. Therefore every case should be given the chance of cure if there is a remote possibility of cure.

Treatment.—Until the cause of cancer is known, prevention is impossible. *Perhaps the most important step in prevention is to urge every* child-bearing woman to nurse her baby. A full period of lactation with each pregnancy offers a degree of protection against cancer and its precursor in some cases—adenosis. *Another method of "protection"* is to avoid overstimulation with estrogenic hormones. Once the disease is present, early and complete removal offers the only means of cure. In *early cases the proportion of five-year cures may reach 70 per cent* or more. The patient with a tumor, even though it appears innocent, is advised by the physician that radical operation may be necessary. This gives the surgeon a free hand. He will remove the growth with the cautery or scalpel by the "nontransplantation" technique (see Chapter 15), if in doubt, and submit it for frozen section. If carcinoma is present, radical mastectomy must be done. We have seen in Chapter 15 that in carcinoma of the breast, the pectoral fascia, pectoral muscles, and axillary and supraclavicular nodes must be removed. The large area of skin removed often requires skin graft and the complete removal of muscles and fascia may lead to temporary restriction of motion. The arm may become edematous due to pressure on the axillary vein or pressure with resultant thrombosis and lymphatic obstruction. The treatment of this complication is discussed in Chapter 11. It is a mutilating procedure but not half so destructive locally or systemically as the carcinoma would be.

The fate of a woman with carcinoma is sealed when she comes to the doctor's office because he can procure an arrestment of the disease only if widespread metastasis has not occurred.

What happens to the patient that has nothing done? One out of four (25 per cent) will survive for five years but there will be practically no cures (one or two spontaneous cures have been reported by good authorities), whereas in the surgery group some will be cured. The scirrhus type is more apt to give a no-treatment five-year survival and also this variety may give the surgeon a false impression concerning the efficacy of five-year arrestment. What happens if x-ray and radium are used? The results will be similar to those when surgery is used, with surgery having a 3 per cent advantage. What does all this mean? Simply this: that no matter whether surgery or x-ray is used, the result depends upon the extent of the growth.

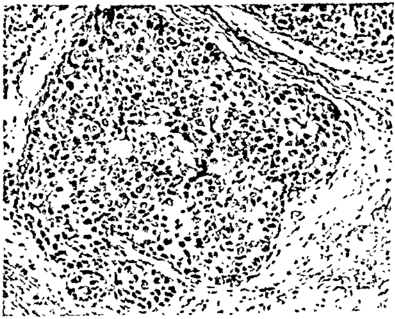

Fig. 160.—Diffuse duct-cell carcinoma of the breast. Also called comedo carcinoma, due to the cellular debris which may be expressed from the duct. The duct wall is greatly thickened and is replaced by malignant cells.

Perhaps the most important factor in prognosis is the stage of the disease at treatment. The Cancer Committee of the American College of Surgeons recommends the following classifications: Stage A—disease limited to the breast; Stage B—questionable involvement of axillary nodes; Stage C—axillary nodes involved; Stage D—Supraclavicular nodes involved; Stage E—Remote metastases present. Obviously the greatest number of the five-year cures will be in Stage A. Curability as well as survival time of patients not cured decreases in Stage B and more in Stage C as axillary lymph node metastases increases. Also local recurrence is more apt to occur in Stage C than in Stage A or B. Furthermore, patients living without clinical evidence of cancer at the end

C. Adair recommends postoperative x-ray treatment and uses the following dosage: If there is a moderate amount of axillary involvement, a total of 1,800 to 2,000 roentgens are used. If there is a large amount of axillary disease with cancer spread over as far as the costoclavicular ligament, 2,000 to 2,250 roentgens are employed (Stage D). The divided dose (Coutard) method is used. Enough should be given to control the lymphatic node spread but not enough to cause edema. Irradiation alone is used in some clinics. The results are *not as good* as in surgery alone or surgery with subsequent x-ray treatment mainly because the axillary nodes cannot be effectively destroyed, although some roentgenologists have obtained excellent results. We have used it as a palliative measure in late inoperable carcinoma (Stage E). It may be indicated in those who cannot stand surgery, although the effects of irradiation are not innocuous. In late, badly ulcerated, and infected carcinoma with general metastasis simple excision is done as a palliative and hygienic measure. It is also done occasionally in women over 75 years of age and those in poor general condition due to associated disease. Postoperative irradiation is used in this group (Stage E).

Other Methods of Treatment.—Bilateral oophorectomy or x-ray castration has been advocated as a complementary or supplementary procedure to radical mastectomy particularly in young women and the premenopausal group, those with acute inflammatory carcinoma (acute carcinosis), those who are pregnant or recently post partum, the more advanced cases with metastasis or recurrent lesions. The influence of estrogenic hormones has been reviewed in this chapter and in Chapter 15. In view of all available information, castration must be regarded as experimental and its merits as yet entirely unproved. We have used the procedure in the type of cases mentioned without any discernible benefit. Several reports of castration in the male with late carcinoma of the breast have been favorable—one states that results equal those of castration in carcinoma of the prostate.

Testosterone propionate has been used in late carcinoma in large doses —200 mg. daily for seven days and 25 mg. three times a week for ten weeks. Implantation of testosterone pellets subcutaneously has also been used. There are no toxic effects. A regression of the primary lesion and of soft parts metastasis and relief of pain does occur. If hypercalcemia is present, this may be aggravated. This therapy should be controlled by daily blood counts, serum calcium, serum phosphorus, alkaline phosphatase determinations, and urinalyses. It is also used postoperatively in doses of 200 mg. per week. There may be virilism, disturbed menstruation, or amenorrhea as a result of its use. We have used the drug in a small number of patients with advanced mammary cancer including two patients with pleural involvement. Our results have been good as to its temporary effect on the growth and relief of pain.

Carcinoma and Pregnancy.—We have reviewed this subject in Chapter 15. Our experience has been that the disease is not curable by any

There is much discussion concerning the relative merits of irradiation, surgery, or combinations. Early, complete, and radical surgery offers the best chance for cure. Reports are available to show that even a simple mastectomy (which we do not condone) will produce 70 to 80 per cent five-year cures or results as good as the radical procedure.

These cases probably have no axillary node involvement (Stage A) and since this cannot be accurately determined without a biopsy of the nodes, the operation of removing the breast or just the growth is dangerous and does not give the patient her best chance. Preoperative irradiation does not add any to the possibilities of cure. In fact, it delays the operation and in this way actually does harm. *Radical mastectomy is the best form*

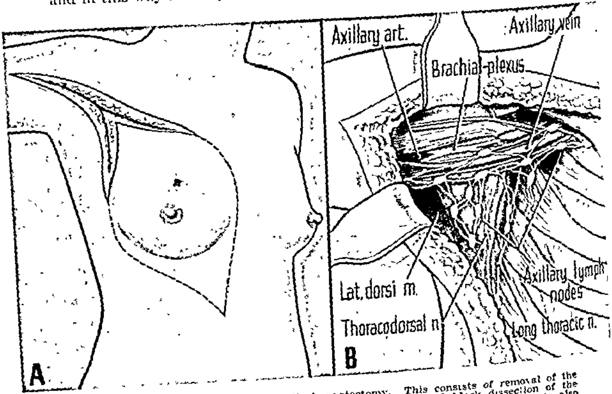

Fig. 161.—Diagram illustrating radical mastectomy. This consists of removal of the breast, the subcutaneous tissue and skin, fascia, muscles, and block dissection of the axillary lymph nodes. If necessary, dissection of the supraclavicular nodes is also carried out. The entire area should be removed in toto so that lymphatics will not be cut across. If sufficient skin remains, as may be the case in small breasts with a very small early lesion, primary closure may be done. If not, secondary skin graft will be necessary.

A. Skin incision. *B*. The pectoralis major and minor muscles and the costocoracoid membrane have been divided and pulled medially and downward to show the lymph nodes. The thoracoacromial artery and vein, long thoracic artery and vein, subscapular artery and vein have been tied and divided.

of treatment available for the cure of mammary cancer. The term radical means complete excision of the primary growth, its extention and its metatases insofar as is possible. This may necessitate (1) exploration of supraclavicular as well as axillary node basins; (2) resection of ribs and cartilages and intercostal muscles along with the pectorals; (3) excision of pleural spread; and (4) even lobectomy. This is as good as surgery plus postoperative irradiation in our hands for Stages A, B, and

Malignant Melanoma

Malignant melanoma of the breast has been reported in current literature and by Deaver and McFarland. It is extremely rare.

Neoplasms of the Male Breast

Chronic cystic mastitis occurs in the male breast in much the same variety as the female. Fibroadenoma and periductal fibroma is seen rarely. Cancer of the male breast is as malignant as in the female. It is usually seen at a later stage and therefore statistics show it to be even more "virulent" than in the female. It is treated by radical mastectomy. We have had good results in this group—five-year cures have been 75 per cent. Two of our patients were colored men.

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form of therapy. We have used three methods of treatment: (1) radical mastectomy followed by supravaginal hysterectomy and bilateral salpingo-oophorectomy; (2) preoperative irradiation, radical mastectomy, and postoperative irradiation; (3) x-ray therapy alone. The effects of irradiation should be theoretically better because the speeded-up growth of cells stimulated by the development of the organ in which the cancer cells live are more susceptible to x-ray therapy. We are now in favor of radical mastectomy and postoperative irradiation—the pregnancy is not disturbed. Castration is not done but testoresone is given.

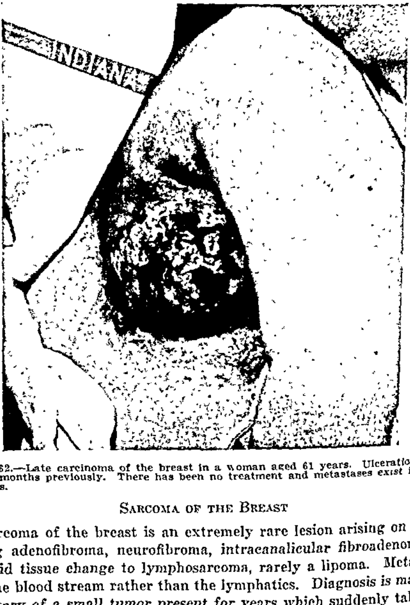

Fig. 162.—Late carcinoma of the breast in a woman aged 61 years. Ulceration began eighteen months previously. There has been no treatment and metastases exist in bones and lungs.

Sarcoma of the Breast

Sarcoma of the breast is an extremely rare lesion arising on a pre-existing adenofibroma, neurofibroma, intracanalicular fibroadenoma, or lymphoid tissue change to lymphosarcoma, rarely a lipoma. Metastasis is by the blood stream rather than the lymphatics. Diagnosis is made on the history of a small tumor present for years which suddenly takes on very rapid growth, reaching an enormous size. Biopsy is the only sure way of making the diagnosis. Treatment is by radical mastectomy except in the case of lymphosarcoma which is amenable to x-ray therapy.

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system is a closed one, lined by endothelium. This tissue, therefore, is of great importance in health and disease—perhaps often the initial seat of disease, with subsequent perivascular involvement.

Blood vessels are are largest as they enter or leave the heart and smallest at the periphery. Lymph vessels increase in size as they approach the veins, into which they empty. The entire system is a closed one although there is some dispute about the spleen, bone marrow, and lymph nodes. The splenic pulp spaces are thought to be the only connection between arteries and veins in this organ (see Chapter 22). Sinusoidal types of vessels are found in the bone marrow and thickened meshworks of capillaries in lymph nodes. It is true, however, that in both of the latter sites blood cells and lymphocytes must enter the circulation by breaking through the walls of vessels.

THE HEART

The mammalian heart pursues a complex course in its development. Like the primitive blood vessels, the heart starts with an interna endothelial tube which becomes the essential component of the endocardium and an external mesodermal layer which gives rise to the myocardium and epicardium.

The heart and its covering, the pericardium, occupy the inferior portion of the mediastinum. It is well protected and cannot be approached with aspiration needle except in a small area which is not overlaid with lung. This area is to the left of the xyphoid cartilage, close to the sternum, in the fourth and fifth interspaces. A few years ago the surgeon did not dare to operate upon the heart. Today he is called upon to suture stab wounds of the heart and thereby prevent fatal hemorrhage.

Congenital Malformations of the Heart and Major Vessels

Congenital cardiovascular defects occur in about 1 per cent of all births. Abbott classified congenital heart disease into three main groups:

Group I. Acyanotic group. No abnormal communications between the right and left side of the heart. Incidence about 25 per cent of cardiac anomalies.

a. Coarctation of the aorta—8%
b. Anomalies of the aortic arch—2%
c. Aortic stenosis—2%
d. Anomalies of semilunar cusps—5%
e. Pericardial defects—2%
f. Displacements of the heart—2%

Group II. Cyanose tardive group. These patients have arteriovenous shunts with arterial blood entering the pulmonary circulation. Cyanosis usually not present but a transient reversal flow may produce cyanosis. Incidence 50% of cardiac anomalies.

a. Patent ductus arteriosus—13%
b. Defects of auricular septum—20%
c. Defects of ventricular septum—17%

Group III. Cyanosis is a prominent feature. Incidence 25% of cardiac anomalies.

a. Tetrology of Fallot—12%
b. Tricuspid atresia—1%
c. Pure pulmonary stenosis—1%
d. Transposition of great vessels—2%
e. Eisenmenger's complex—5%
f. Persistent truncus arteriosus—1%
g. Complete septal defects—1%
(cor triloculare and biloculare)

Chapter 17

CIRCULATORY SYSTEM

Embryology and Anatomy

Early authorities stated that blood vessels and blood cells arise from a tissue termed the angioblast (His). It is probably mesodermal in origin and is first seen in the yolk sac. The solid cords of angioblast soon hollow out, leaving the peripheral cells as the endothelium and the inner cells as the primitive blood cells or mesoameboids (Minot). Authorities do not agree as to the exact origin of the vascular system. Many observers state that the first blood vessels and cells appear in the area vasculosa which surrounds the embryonic body and overlies the cavity of the yolk sac. The peripheral mesenchyme which spreads out between the ectoderm and mesoderm gives rise to groups of basophil cells (blood islands) connected by strands of elongated cells which are transformed into endothelial tubes. The endothelium secretes a liquid, the primitive blood plasma which fills the tubes. The first blood elements or primitive blood cells are free mesenchymal cells. These free cells in the connective tissue become the first red and white blood cells; others become the endothelium of blood vessels; still others form lymph vessels. These primitive vessels join to make the endothelial lining of arteries, veins, and lymphatics. Larger vessels acquire outer layers. Capillaries do not, so that they may have a free exchange with the connective tissue spaces. Thus from connective tissue the real vascular tissue of the body originates. By the union of isolated endothelial spaces a vascular network results, which ultimately permeates the entire body. This growth is by budding or sprouting with the formation of loops and off-shoots. The primitive vessels may serve as arteries or veins (Sabin), probably accounting for many capillary malformations (hemangioma), anomalous vessels, and enlargements of organs. Vessels have three coats. The outer coat *(adventitia)* is composed of connective tissue. Sympathetic nerves are found here. They come off at various levels from peripheral nerves—except in the larger vessels, where the nerves come directly from the sympathetic ganglia. The blood supply to the vessel (vasa vasorum and vasa venorum) is found in the adventitia. The vaso vasorum originate from near-by small arteries and form a dense capillary network in the adventitia, penetrating to the media. In veins they penetrate to the intima and the veins of these vessels open into the lumen of the vessels they drain. Lymphatics are also present in the larger vessels. The middle coat *(media)* is formed of muscle and elastic fibers in varying proportion in the different sized vessels. The large arteries have little muscle, mostly elastic tissue, allowing for great expansion. The arterioles have a relatively thick muscle coat to permit vasomotor control. The capillaries have no muscular coat but have Rouget cells which are probably modified endothelial cells and are capable of causing contraction. The boundary between the tunica intima and media is formed by the internal elastic membrane which is most noticeable in medium sized arteries. The inner coat *(intima)* consists of endothelium and prevails throughout the vascular system.

It has been estimated by Krogh that there are over 700 capillaries per cubic millimeter in normal human muscle. He states that these capillaries placed end on end would extend over 100,000 kilometers (62,000 miles). Since the muscles constitute only about 40 per cent of the weight of the healthy adult body, it would be conservative to estimate the total length of all the capillaries in the rest of the body at 38,000 miles; therefore we may conclude that there are more than 100,000 miles of blood capillaries. The lymphatic capillaries and vessels are almost as numerous. The entire

Fig. 163.—Congenital anomalies of the heart and great vessels. Case of an adult with a thrombotic occlusion of both pulmonary arteries secondary to severe pulmonary atherosclerosis which, in turn, was probably sequential to a patent interventricular septum. Associated anomalies were a right-sided arch of the aorta and an anomalous left subclavian artery springing from the descending portion of the aorta and resulting in a vascular ring about the esophagus and trachea. There were also a patent foramen ovale and a large interventricular septal defect. Cyanosis and dyspnea increased abruptly twenty-eight days before death probably due to the fact that the pressure in the pulmonary artery equalled that of the systemic pressure and much blood flowed back from right to left not being oxygenated. Two other factors contributed to the cyanosis and dyspnea: (1) anoxic anoxemia due to the vascular ring compression of the trachea and chronic interstitial pneumonia; (2) bilateral pulmonary artery thrombosis.

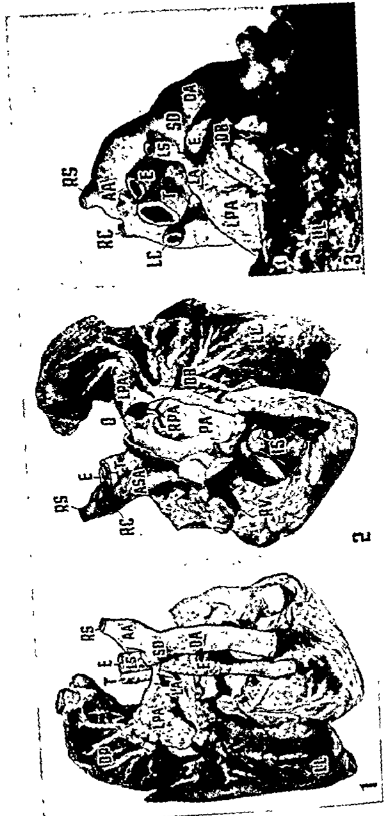
This was a case of a man 45 years of age who complained of being short of breath and of having heart trouble since early childhood. When brought to the hospital he was extremely ill, deeply cyanotic, and dyspneic. His blood pressure was 105 systolic, 70 diastolic. The circulation time, arm-to-lung, was 7.5 seconds. The arm-to-tongue time was prolonged to 27 seconds. Normal should be between 9 and 16 seconds. The venous pressure was 17 cm. of water. Five electrocardiograms taken during his hospital course showed a left axis deviation with delayed intraventricular conduction and auricular fibrillation.

1. Photograph taken from behind, showing the greatly dilated pulmonary artery and the posterior portion of the vascular ring. *AA*, arch of aorta; *DA*, descending aorta; *DP*, dilated branches of left pulmonary artery; *E*, esophagus; *LA*, ligamentum arteriosum; *LPA*, left pulmonary artery; *LS*, left subclavian artery; *RS*, right subclavian artery; *SD*, saccular dilatation; *T*, trachea; *LL*, left lung.

2. Photograph of the specimen from the front with a window cut in the right ventricle to demonstrate the septal defeat. The pulmonary artery has been opened and reflected to show the great dilatation present and the occluding mass on the left pulmonary artery. Note the greatly thickened right ventricular wall.

ASA, ascending aorta; *DB*, dilated branches of *LPA*; *E*, esophagus; *IS*, interventricular septal defect; *LL*, left lung; *LPA*, left pulmonary artery; *O*, occluding thrombus in *LPA*; *PA*, pulmonary artery (greatly dilated); *RC*, right common carotid artery; *RPA*, right pulmonary artery; *RS*, right subclavian artery; *RV*, right ventricle; *T*, trachea.

3. Photograph of the specimen taken from above and behind. It shows the vascular ring above the esophagus and trachea. It shows also the greatly dilated and thrombosed left pulmonary artery and its branches. *AA*, arch of aorta; *DA*, descending aorta; *DB*, dilated branches of pulmonary artery; *E*, esophagus; *LA*, ligamentum arteriosum; *LC*, left common carotid artery; *LL*, left lung; *LPA*, left pulmonary artery; *LS*, left subclavian artery; *RC*, right common carotid artery; *RS*, right subclavian artery; *SD*, saccular dilatation; *T*, trachea.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RV
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LS
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1

circulation must be balanced by an equal volume of unsaturated blood entering the pulmonary circulation. A unilateral shunt would lead to a diminishing blood volume in either pulmonary or the systemic circulation.

Incomplete Development of Heart and Great Vessels

Rarely there is a tendency toward doubling due to incomplete fusion of the paired primordia. More common congenital abnormalities are an incomplete ventricular septum due to a faulty development of the septum membranaceum and persistent foramen ovale due to improper fusion of the septum primum and secundum. *Arey states that the latter occurs* in one out of every four individuals, but actual mingling of blood or inconvenience to the individual is unusual because the communication is small or because septal folds are pressed together during atrial contraction, acting as a valve. When the opening is large, there is intermingling of blood, causing cyanosis—"blue baby." Valvular anomalies occur in the atrioventricular and semilunar valves.

Due to the extensive work of Taussig, many other types of teratologic and congenital defects and deformities have been described and their clinical features studied. Operations for their relief have been devised by Blalock, Gross, Crafoord, Fauteux, Potts, and many others. Some of these procedures, while still in the experimental stage, are very promising.

Patent interventricular septa have been partially repaired by Murray as follows:

> A strip of fascia lata about ¾ inch wide was secured. A silk suture was attached on one end and this was threaded on a straight sewing needle four inches long. At a point slightly to the right of the descending branch of the left coronary just distal to the annulus fibrosis the reversed needle was passed through the anterior wall of the heart and then through the posterior wall. The suture was anchored to the epicardium.

Tricuspid atresia has been benefited by aortic-pulmonary anastomosis. *The physical findings are identical with those of the tetralogy of* Fallot except that there are (1) left axis deviation in the electrocardiogram (the only lesion that produces cyanosis and has this); (2) hypertrophy of the left ventricle; (3) hypoplasia of the right ventricle by x-ray studies.

When pulmonary stenosis involves the pulmonary valve itself (about 10 per cent) rather than the pulmonary conus (which is the site in over 90 per cent of the cases), a valvulotome may be inserted through an incision in the wall of the right ventricle and used to divide the pulmonary valves.

Methods Used in the Diagnosis of Various Types of Congenital Cardiac Anomalies

Symptoms and Signs.—The importance of murmurs and their connotations are different in adults and children. In children the appear-

Formerly anomalies of the heart and its major vessels were not amenable to surgical aid. Such is not the case now, although many abnormalities are not yet within the realm of surgical attack. The following discussion will consist of first a review of experimental and clinical work on the rarer types and second the more common varieties. In all kinds there are apt to be associated anomalies in the heart and elsewhere.

Abnormal Positions of the Heart and Great Vessels

Ectopia Cordis.—Ectopia cordis is a protrusion of the heart through an opening in the thoracic wall. This anomaly may cause serious circulatory phenomena due to lack of restraint of the normal heart. Usually only a thin layer of skin covers the heart and sometimes even this is absent (see Chapter 20—Celomic Cavity). The treatment consists of the formation of skin flaps in the latter instance. Cartilage grafts from the eighth and ninth costal cartilages may be used to bridge the defect in the upper sternum and ribs.

Dextrocardia.—Dextrocardia is a transposition of the heart and its vessels. It may be associated with no other anomalies and it may cause no symptoms. However, it is often seen with a general inversion of all the viscera. This is known as *situs inversus totalis* or *situs inversus viscerum*. This abnormality is, in turn, not infrequently accompanied by an agenesis of the accessory nasal sinuses and maldevelopment of the bronchi and the pancreas. The Kartagener syndrome includes situs inversus, bronchiectasis, and sinusitis. However, fibrocystic disease of the pancreas and gall bladder disease, including atresia of the bile ducts (in two of our cases) have also been found often to be noncoincidental.

Complete Transposition of Aorta and Pulmonary Artery.—Complete transposiiton of the aorta and the pulmonary artery if "uncorrected" is incompatible with life. The aorta arises from the ventricle which receives systemic venous blood, and the pulmonary artery arises from the ventricle receiving oxygenated blood. Thus the left ventricle pumps blood through the pulmonary artery to the lungs and this blood returns by way of the pulmonary veins to the left auricle. The right ventricle propels blood into the aorta, while the right auricle receives impure blood from the systemic veins. Usually there are associated septal defects or other abnormalities so that some oxygenated blood goes into the systemic circulation, permitting survival. Attempts have been made experimentally to correct the "uncorrected" condition by anastomosing the pulmonary vein to the superior vena cava, or by producing an interatrial septal defect. The latter operation might also be useful in mitral stenosis as observed in patients with a mitral stenosis associated with a patent foramen ovale (Lutembacher syndrome). In "uncorrected" transposition, it must be taken into consideration in shunts which are created that the volume of oxygenated blood shunted into the systemic

measures 20 volumes per cent. That is 20 volumes in each 100 c.c. of arterial blood. With the catheter in the right atrium, the sample of blood (mixed venous blood) shows 15 volumes per cent or 15 c.c. of oxygen in each 100 c.c. of venous blood. The total oxygen consumption as tested is 300 c.c. per minute. Thus, 5 c.c. of oxygen is taken up by the tissues per 100 c.c. of blood. The patient consumes 300 c.c. of oxygen per minute. Three hundred divided by five will give the units of 100 c.c. of blood flowing from the aorta (since aorta and femoral artery oxygen content are about the same) to the right atrium, or the *total systemic blood flow;* in this case, 60 units of 100 c.c. or 6,000 c.c. per minute.

In the lungs the oxygen goes into the blood instead of out of it. If the catheter tip is placed in the pulmonary artery, the blood sample may show 15 volumes per cent and that from the femoral artery, 20 volumes per cent (and this is practically the same as in the pulmonary vein). Thus 5 c.c. of oxygen has been added to each 100 c.c. of blood flowing through the lungs. The *pulmonary flow in each case is*

$$\frac{300}{20 - 15} \times 0.1 = 6 \text{ liters per minute.}$$

The volume of flow through single, one-direction shunts may be estimated by calculation of the difference between the pulmonary and peripheral flows. If there is a shunt in both directions more complicated formulas are needed.

The ratio of the effective pulmonary blood flow to the total systemic flow determines the degree of oxygen saturation in arterial blood.

The *pulmonary capillary flow* is determined by a method involving the equilibration of carbon dioxide with pulmonary capillary blood, sampling carbon dioxide content in alveolar air, and determination of carbon dioxide production. By comparing pulmonary artery with pulmonary capillary flow, the flow through the collateral vessels or through an artificial or congenital ductus arteriosus may be estimated (Bing).

The standard exercise test compares ratios of oxygen consumption to respiratory minute volume during rest and exercise. Normally oxygen consumption increases from rest to exercise. In conditions where the pulmonary flow is fixed (for example, pulmonary stenosis) the ratio usually declines.

The *oximeter* is an instrument which measures the oxygen saturation in peripheral arterial blood by means of a photoelectric cell attached to the pinna of the ear. It can be used in connection with the exercise test and is also useful in differentiating anoxemia due to venous-arterial shunts from deficient arterial saturation due to oxygen absorption difficulties resulting from pulmonary disease. In the latter case oxygen solution rises within one minute to full saturation when 100 per cent oxygen is inhaled. In shunts the time required will be much longer, and full saturation is rarely obtained.

ance of a murmur may suggest an abnormality, but the heart is too small, the blood pressure too low, and the chest wall too thin for the murmur to be of specific diagnostic aid. Useful diagnostic signs are unusual murmurs and thrills, cyanosis, clubbing of fingers, and alteration in size, shape, and position of the heart.

X-ray and Fluoroscopy.—X-ray and fluoroscopy frequently help make the diagnosis in conjunction with the information derived from the symptoms and signs.

Angiocardiography.—Angiocardiography is the visualization of the heart and great vessels with opaque media. This method may be briefly summarized as follows: (1) The patient is given a small capsule of one of the barbiturates. (2) The heart rate and blood pressure are determined. (3) The patient is tested for sensitivity to Diodrast, a brand of iopracyl, and if sensitivity is present, antihistamine drugs may be used or the drug may be employed in weaker concentration. (4) Decholin sodium solution, 5 c.c., is added to 20 c.c. of physiological saline and injected into an arm vein with the arm elevated to 45 degrees. The interval between the beginning of the injection and the onset of the bitter taste is measured by a stopwatch. This gives the arm-to-tongue circulation time and if less than 10 seconds the lung circulation time will be short—3 to 4 seconds. (5) To obtain arm-to-lung circulation time, 0.5 c.c. of ether is added to 20 c.c. of physiological saline and injected. The interval between the time of injection and the detection of ether on the patient's breath is the arm-to-lung circulation time. (6) The approximate time of opacification of the right ventricle and pulmonary arterial line and of the left ventricle and aorta is obtained by deducting one second from the arm-to-lung and the arm-to-tongue circulation times. (7) A concentration solution of Diodrast (a brand of iopracyl), 70 per cent by weight/volume, usually about 40 c.c. for adults, is injected. The duration of injection should be between 1½ to 2 seconds.

An added test is the combined use of angiocardiography and electrocardiography which permits synchronization of the various waves with the actual visualization of the heart.

Physiological Studies.—The most useful are catheterization of the heart, measurement of pulmonary capillary flow, a standard exercise test, and oximetry.

Venous catheterization gives much information. The position of the catheter should be followed by the use of the fluoroscope. Blood samples and blood pressures are obtained by means of the catheter from the cardiac cavities, blood vessels coursing to and from the heart, and from a peripheral artery. The volume of blood flowing through the pulmonary artery (pulmonary artery flow), the intracardiac shunt, and the systemic blood flow may be calculated by the Fick principle from the oxygen content of the blood samples (see Chapter 13): Oxygen in the femoral artery

Pulmonary Stenosis or Atresia and Associated Defects

These anomalies result in a decreased volume of blood to the lungs for oxygenation. The result is cyanosis due to the anoxemia and compensatory polycythemia—the "blue baby." We shall see in Chapter 19 that cyanosis is due to the presence of reduced hemoglobin in the circulating blood. When venous blood is shunted into the arterial tree, cyanosis results. Cyanosis is dependent not only on the volume of blood going to the lungs for oxygenation but also on the height of the hemoglobin (less than 5 grams of reduced hemoglobin will not produce clinical cyanosis; therefore, the hemoglobin must be higher than 5 grams), the volume of

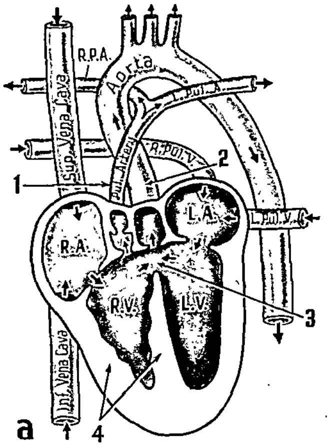

Fig. 164a.—Tetrology of Fallot. The four features of the tetrology of Fallot are (1) pulmonary stenosis, (2) dextroposition of the aorta, (3) a patent interventricular septum or at least an intraventricular septal defect, and (4) right ventricular hypertrophy. The arrows show the course of the circulation in the tetrology of Fallot.

R.A., Right auricle; *R.V.*, right ventricle; *L.A.*, left auricle; *L.V.*, left ventricle; *R.P.A.*, right pulmonary artery.

Note that the dextroposition of the aorta permits it to receive blood from both ventricles. Blood reaches the right auricle through the vena cavae and then it goes from the right auricle to the right ventricle. Then part of the blood goes through the narrow pulmonary artery and part directly into the aorta. The small volume of blood going through the pulmonary artery is oxygenated and returned to the left auricle and thence to the left ventricle. Blood from the left ventricle and some from the right ventricle is propelled into the aorta from which it is distributed throughout the body.

TABLE XIII

CHARACTERISTIC DATA EXPECTED FROM CATHETERIZATION OF THE HEART IN VARIOUS CONDITIONS
(Modified from Burchell and others: Proc. Staff Meet., Mayo Clin., 1948.)

	PRESSURES		OXYGEN CONTENT OF BLOOD		
	RIGHT VENTRICLE	PULMONARY ARTERY	RIGHT ATRIUM	RIGHT VENTRICLE	PULMONARY ARTERY
Normal	25/2	25/8	Equals venae cavae	Equals right atrium + *or* – 0.5%	Equals right ventricle
Cardiac disease					
Atrial septal defect	Slight increase	Slight increase	Increase over venae cavae	Like right atrium	Like right ventricle
Ventricular septal defect	Normal or increased	Normal or increased	Normal	Exceeds right atrium	Equals right ventricle
Patent ductus arteriosus	Normal or increased	Normal or increased	Normal	Normal	Exceeds right ventricle
Tetralogy of Fallot	Increased	Diminished	Lower than normal	Equals or exceeds right atrium	Equals right ventricle
Eisenmenger complex	Increased	Increased due to arteriolar changes in pulmonary vessels	Normal	Exceeds right atrium	Exceeds right ventricle
Pulmonary stenosis without septal defects	Greatly increased	Greatly diminished	Normal	Equals right atrium	Equals right ventricle
Essential pulmonary hypertension	Increased	Increased	Normal	Equals right atrium	Equals right ventricle

Some additional information *concerning various* congenital anomalies of the heart is as follows:

Tetralogy of Fallot.—The pulmonary artery flow is decreased. Collateral circulation is marked to the lung. The intracardiac shunt is from right to left. The exercise test shows a fall in oxygen consumed per liter of ventilation and a decline in peripheral arterial oxygen saturation. Breathing pure oxygen test. Peripheral arterial saturation rises over several minutes and full saturation is not reached.

Ventricular Septal Defect.—Exercise test—oxygen consumed per liter of ventilation increases and oxygen saturation of peripheral blood falls.

Patent Ductus Arteriosus.—Exercise test—oxygen consumed per liter of ventilation and oxygen saturation in peripheral blood remains constant.

Eisenmenger Complex.—The intracardiac shunt is from right to left due to increased resistance in pulmonary vascular bed.

Miscellaneous Data.—On a number of occasions the aorta has been catheterized through a patent ductus arteriosus. Many times in catheterizations of the heart anomalous pulmonary venous drainage is encountered. These anomalous veins may drain into the superior vena cava or the innominate veins; rarely, also into the inferior vena cava. The diagnosis is made by having the catheter enter the pulmonary vein directly from the superior vena cava and by finding a high oxygen content in the blood taken from the systemic vein. A pulmonary stenosis with an intact ventricular septum but with an atrial septal defect may be diagnosed as an entity. Sometimes in pulmonary stenosis without septal defects there is a marked increased pressure in the right ventricle which may exceed radial or brachial artery systolic pressure.

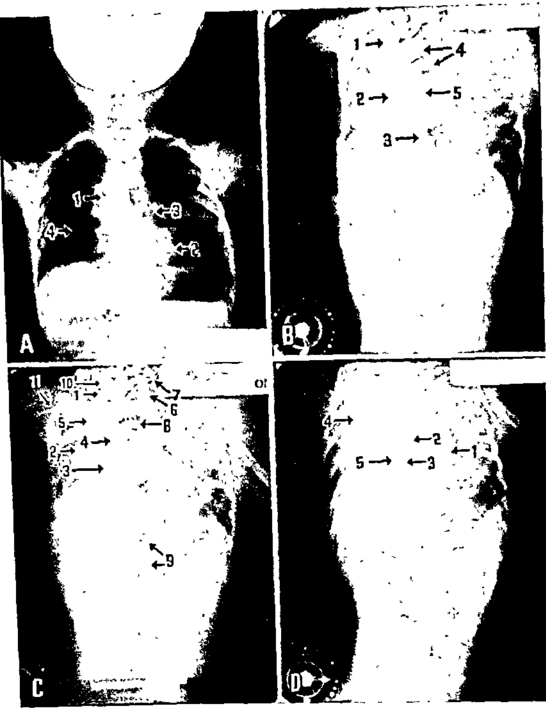

Fig 164b — A Plain posteroanterior roentgenogram of heart with barium swallow showing dextraposed ascending aorta (*1*), elevated apex (*2*), diminutive main pulmonary artery salient (*3*), and reduced peripheral pulmonary arterial markings in the lungs (*4*)

B Left anterior oblique angiocardiogram one second after injection of 70 per cent Diodrast showing opacification of superior vena cava (*1*), right atrium and right ventricle (*2*), inferior vena cava (*3*), simultaneous filling of overriding aorta and pulmonary arteries (*4*), and slight spill of dye through the high interventricular septal defect into left ventricle (*5*).

C. Left anterior oblique angiocardiogram at three-second interval. Superior vena cava (*1*), right auricle (*2*), right ventricle (*3*), stenotic infundibulum of right ventricle (*4*), aorta (*5*), left common carotid (*6*), left subclavian artery (*7*), poststenotic left dilatation of pulmonary artery (*8*), arteries to abdominal viscera (*9*), innominate artery (*10*), right subclavian artery (*11*).

D. Left anterior oblique angiocardiogram at seven seconds. Pulmonary veins (*1*), left atrium (*2*), left ventricle (*3*), reopacified aorta from left ventricle (*4*), interventricular septum (*5*).

venous blood shunted into the systemic circulation, the rate of utilization of oxygen by the peripheral tissues, and the extent of the aeration of blood in the lungs. The latter is obviously of great importance and depends on the vital capacity, the rate of blood flow through the lungs, the partial pressure of the oxygen in the inspired air, and specific pulmonary factors. Lundsgaard and van Slyke showed that these specific factors ("a" factors) are noted in cases of polycythemia. In such cases secondary changes occurred in the lungs of such a nature that not all the blood passing through the lungs was in effective contact with the oxygen in the alveoli. This is proved by the fact that in almost all cases of polycythemia, cyanosis may be improved by the prolonged inhalation of oxygen.

If the volume of blood going to the lungs is diminished, cyanosis results. In pulmonary atresia, in which the circulation to the lungs is by way of the ductus arteriosus, the closure of the ductus results in death. The diminished volume of blood to the lungs is seen in the following types of anomalies.

1. Single ventricle with a rudimentary outlet chamber. Usually the aorta arises from the common ventricle and is of good size; the pulmonary artery arises from the rudimentary outlet chamber and is small. Cyanosis results. If the vessels are transposed, a large volume of blood goes to the lungs for oxygenation and a smaller volume to the systemic circulation. Under such circumstances there will be no cyanosis but symptoms like those of coarctation which will be described later.

2. Truncus arteriosus. If the pulmonary arteries are given off directly from the aorta or heart, there is no cyanosis. If they fail to arise from the heart or connect with the aorta and the circulation to the lungs is by way of the bronchial arteries, a smaller volume of blood reaches the lungs and cyanosis results.

3. Tetralogy of Fallot. This consists of pulmonary stenosis, dextroposition of the aorta, interventricular septal defect, and right ventricular hypertrophy. The pulmonary stenosis consists of a narrowing of the pulmonary orifice and the pulmonary conus of the right ventricle. The aorta rises from the left ventricle and partially overrides the right ventricle; the aortic septum cannot meet the ventricular septum, and therefore, there is a high septal defect. It is difficult for blood to be expelled from the right ventricle due to the stenosis of the pulmonary artery, and, therefore, the right ventricle hypertrophies. The aorta receives blood from both ventricles. The ductus and foramen ovale are closed. A large volume of blood is returned to the right atrium and ventricle and a lesser amount to the left side of the heart.

4. Complete pulmonary atresia is compatible with life only if the ductus arteriosus remains open or the bronchial arteries establish sufficient collateral circulation.

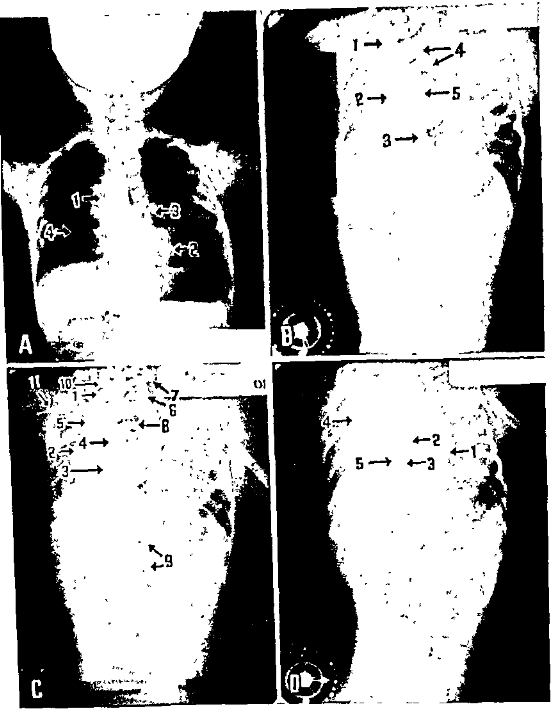

Fig. 164b—A Plain posteroanterior roentgenogram of heart with barium swallow showing dextraposed ascending aorta (1), elevated apex (2), diminutive main pulmonary artery salient (3), and reduced peripheral pulmonary arterial markings in the lungs (4)

B. Left anterior oblique angiocardiogram one second after injection of 70 per cent Diodrast showing opacification of superior vena cava (1), right atrium and right ventricle (2), inferior vena cava (3), simultaneous filling of overriding aorta and pulmonary arteries (4), and slight spill of dye through the high interventricular septal defect into left ventricle (5).

C. Left anterior oblique angiocardiogram at three-second interval. Superior vena cava (1), right auricle (2), right ventricle (3), stenotic infundibulum of right ventricle (4), aorta (5), left common carotid (6), left subclavian artery (7), poststenotic left dilatation of pulmonary artery (8), arteries to abdominal viscera (9), innominate artery (10), right subclavian artery (11).

D. Left anterior oblique angiocardiogram at seven seconds. Pulmonary veins (1), left atrium (2), left ventricle (3), reopacified aorta from left ventricle (4), interventricular septum (5).

5. Complete transposition of the great vessels. In this anomaly there is complete transposition of the great vessels as previously described. The pulmonary artery arises from the left ventricle and the aorta from the right ventricle. Blood goes to the lungs from the left ventricle through the pulmonary artery and is returned to the left auricle by the pulmonary veins. The right ventricle sends blood through the aorta to the

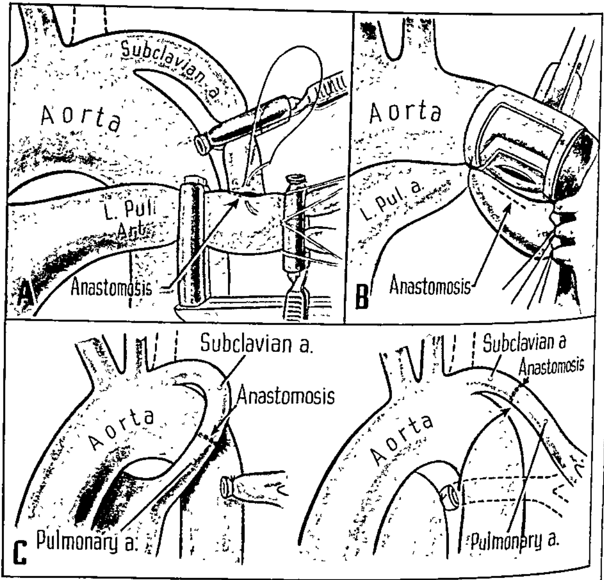

Fig. 165.—The treatment of pulmonary stenosis. Diagrams illustrating various operations which are designed to increase the pulmonary blood flow. The shunt as originally devised by Blalock and Taussig consists of anastomosing the subclavian artery with the pulmonary artery on the left side. In dextropositions of the aorta the innominate artery may be used. *A.* The anastomosis is made end to side as illustrated in the diagram. *B.* The Potts method of producing an artificial ductus arteriosus by anastomosing the aorta with the pulmonary artery with the use of the ingenious Potts clamp. A variation of this is the anastomosis of the pulmonary artery and the ascending aorta. *C.* Other methods employed in shunting the systemic blood into the pulmonary circulation. A branch of the pulmonary artery may be divided and the proximal end anastomosed to the proximal end of the subclavian artery, or the distal end of one pulmonary artery may be anastomosed to the proximal end of the subclavian artery. These are a few of the variations of the methods employed in supplying the lungs with sufficient blood by using one of the larger arteries of the systemic circulation; in other words, producing an artificial ductus arteriosus.

systemic circulation and this is returned to the right atrium via the venae cavae. Thus there is really a transposition of the pulmonary artery and the aorta but not of the vena cava or pulmonary veins. Oxygenated blood has a difficult time in reaching the systemic circulation. Indeed this would not be possible unless there were associated septal defects (auricular, ventricular, or both) or other abnormalities (patent ductus arteriosus, partial transposition of great veins). Recently Blalock and Hanlon have created auricular septal defects surgically and performed anastomosis between the subclavian and pulmonary arteries.

6. Tetralogy of Fallot of the Eisenmenger type. There is dextroposition of the aorta, interventricular septal defect, large right ventricle, and normal or increased size rather than stenosis of the infundibulum and pulmonary valve and artery. Cyanosis is said to be due to secondary changes in the pulmonary vascular bed or the alveolar plexuses, or, due to the increased pressure in the pulmonary circulation, more impure blood may be shunted from the left to the right ventricle. Surgery is not indicated in the Eisenmenger type.

7. Aortic atresia causes difficulty in pumping blood to the systemic circulation. Moreover, most of the blood reaching the systemic system is pumped through the ductus arteriosus before it has been to the lungs for oxygenation.

When there is an inadequate flow of blood to the lungs, surgery may be used to "short-circuit" around the obstruction. The clinical diagnosis, according to Taussig, rests upon three important features: (1) x-ray evidence that the pulmonary artery is small, (2) clinical and roentgenological evidence of absence of congestion in the lung fields, (3) absence of visible pulsation in the lung fields as observed under the fluoroscope. The typical case of the tetralogy of Fallot is not difficult to diagnose. In borderline cases of persistent cyanosis surgery is indicated, and if there is doubt, Blalock advises that the pressure in the pulmonary artery may be measured by using a needle and water manometer. Usually the pressure will be 150 to 240 mm. of water. If the pressure is more than 300 mm. of water, the operation is unnecessary. Because this approaches aortic pressure and usually indicates an absence of the ventricular septum, blood would not flow into the pulmonary artery in such cases. If, however, the systemic arterial pressure is higher, a shunt may be created even with pulmonary artery pressures of 500-600 mm. of water.

The operation seeks to divert blood from one of the major systemic arteries to one of the pulmonary arteries. Usually the approach is on the right side where the innominate artery is located. If the aorta descends on the right, the innominate will be on the left. Many surgeons prefer the left side in left aortic arch and the right side in right aortic arch, preferring the subclavian if possible. By exposing the innominate, the subclavian, common carotid, or innominate may be used, depending

on the existing inadequacy of the flow of blood to the lungs and the sizes of the available vessels. By this method an artificial ductus arteriosus is made and in the tetralogy of Fallot some of the blood which is pumped into the aorta will reach the lungs through the artificial ductus and thereby the left ventricle will receive more blood, better oxygenated, and the right side of the heart will receive less.

The results have been encouraging according to Blalock. There has been an increase in oxygen content of the arterial blood, a decrease in the oxygen capacity, an increase in the oxygen saturation of the arterial blood, a decrease in the red blood cell count, a diminution of the hemoglobin and the hematocrit reading, a decrease in the patient's disability, and an improvement in the patient's ability to exercise. The immediate mortality rate is 23 per cent. The arteries may be anastomosed in the following ways: end to side; the proximal end of the systemic artery with the distal end of a pulmonary artery (the blood pressure in the pulmonary artery is less than half that in the systemic due to low peripheral resistance; the flow of blood depends upon the relative pressure between the systemic and pulmonary circulations); the proximal end of the subclavian or common carotid with the divided proximal end of the pulmonary arteries to an upper lobe of one of the lungs; the side of the aorta with the left pulmonary artery; the side of the aorta to the side of the main pulmonary artery. Potts, Smith, and Gibson anastomose the pulmonary artery to the aorta by means of special clamps. If the patient has pronounced polycythemia, some blood loss (about 1 per cent of body weight) is helpful. Surgery is not indicated in cor biloculare, cor triloculare, persistent truncus arteriosus, and Eisenmenger's complex.

Aortic Arch Anomalies

Most textbooks of embryology, pathology, and anatomy mention the occurrence of abnormal developments in the aorta and its branches. Fig. 166 shows the embryological development. Recently Gross, Blalock, Crafoord, and others have shown the importance of recognizing these malformations so that surgical treatment may be instituted. The following is a classification of the more common types of aortic arch anomalies as listed by Gross.*

Classification of Aortic Arch Anomalies With Notes on Diagnosis and Treatment

I. Right Aortic Arch.—
   A. Situs inversus viscerum—usually no symptoms.
   B. Right aortic arch without inversion.
      1. Anterior type—Arch is anterior to the trachea. Descending aorta is right sided. Rare anomaly.
      2. Posterior type—Arch passes to the left behind esophagus. Descending aorta courses to the right or normal left side position.
         a. Right aortic arch in which the left subclavian artery arises last from the arch and crosses behind the esophagus may produce dysphagia by pressure of left subclavian posteriorly. This could be divided.

*Gross and Ware: Surg., Gynec. & Obst., 1946.

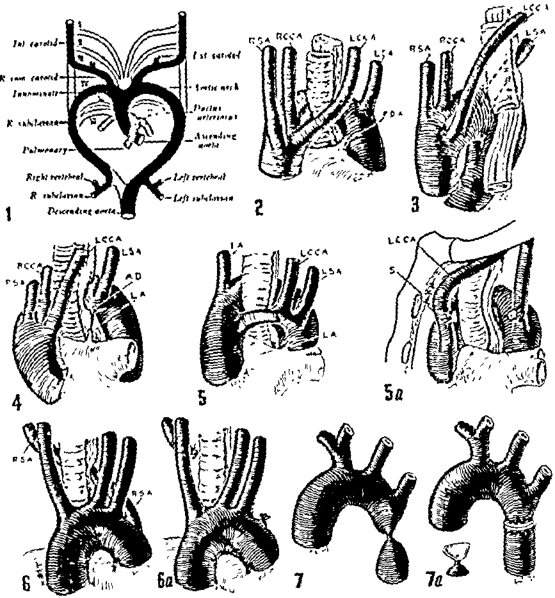

Fig 166.—Anomalies of the aortic arch. *1* is a diagram showing the transformation of the human aortic arches. The scheme in the ventral view is shown with all vessels spread to the same plane. (Redrawn from Arey; modified from Congdon.) *2* is a diagram of a right aortic arch with no vessel from the arch crossing behind the esophagus Left common carotid artery compressing the front of the trachea. Pulmonary artery drawn tightly against the trachea by the ductus arteriosus. *LCCA*, Left common carotid artery, *LSA*, left subclavian artery, *PDA*, patent ductus arteriosus, *RCCA*, right common carotid artery, *RSA*, right subclavian artery. *3* is a diagram of a right aortic arch with left subclavian artery arising last from the arch and crossing behind the esophagus. *LCCA*, Left common carotid artery; *LSA*, left subclavian artery *RCCA*, right common carotid artery; *RSA*, right subclavian artery. *4* is a diagram of a right aortic arch with persistent left aortic diverticulum giving rise to the left subclavian artery and the ligamentum arteriosum. Frequently the aortic diverticulum is longer than is indicated in this diagram *AD*, Aortic diverticulum; *LA*, ligamentum arteriosum, *LCCA*, left common carotid artery; *LSA*, left subclavian artery, *RCCA* right common carotid artery; *RSA*, right subclavian artery. *5* is a diagram of a left double aortic arch. The ascending aorta divides into two limbs which subsequently join and form the descending aorta. The esophagus and trachea are compressed. *5a* shows a method of surgical treatment. The ligamentum arteriosum has been divided to allow the pulmonary artery to fall forward. The anterior or left limb of the double arch has been severed between the origins of the left common carotid artery and the left subclavian artery. The left common carotid artery is then tacked to the back of the sternum to keep it off of the trachea. *6* shows an anamolous right subclavian artery which arises from the left side of the aortic arch and presses on the posterior wall of the esophagus. *RSA*, right subclavian artery. *6a* shows a method of surgical treatment for the dysphagia. The subclavian artery has been divided and esophageal pressure thereby has been relieved *7* is a diagram illustrating coarctation of the aorta with a high degree of constriction and obstruction just beyond the origin of the left subclavian artery. *7a* shows a method of treatment by the excision of the narrow segment and end-to-end suture of the aorta. Inset shows the excised portion possessing a very small lumen. (Diagrams slightly modified from Gross, R. E., and Ware, P. F.: Surg., Gynec. & Obst. 83: 435, 1946.)

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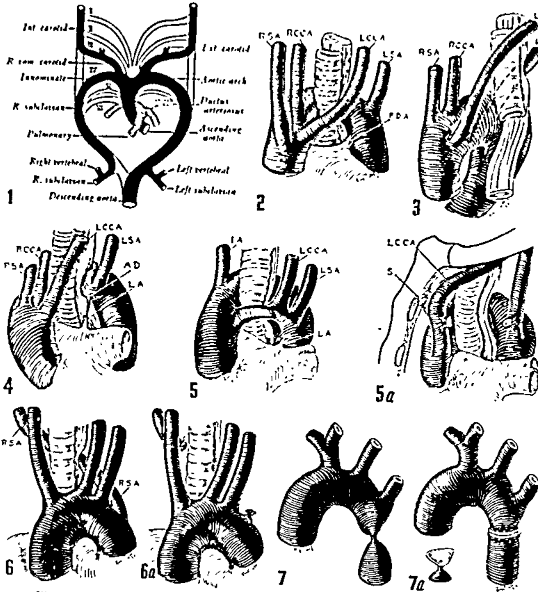

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b. Right aortic arch in which no vessel arising from the arch crosses the midline posterior to the esophagus. A vessel may pass in front of the trachea. The left common carotid may pass in front of the trachea and compress it. The left subclavian and left common carotid may arise from a left innominate. The pulmonary artery is pulled back against the trachea due to the posteriorly displaced arch and the resultant pull on the ligamentum arteriosum (or patent ductus arteriosus). Rarely it may be necessary to divide the compressing left common carotid or the ligamentum arteriosum (or patent ductus arteriosus).

c. Right aortic arch with a persistent left aortic diverticulum giving origin to the left subclavian artery and ligamentum arteriosum. The important part of this anomaly is the aortic diverticulum which is an outpocketing of the distal part of the arch and which gives rise to the left subclavian artery and to the ductus arteriosus (or the ligamentum arteriosum). If the aortic diverticulum presses on the esophagus and interferes with swallowing, it could be removed and the first part of the subclavian excised.

II. Double Aortic Arch.—The originally paired dorsal aortae may persist as a double aorta or double arch such as is found normally in reptiles (Arey). The ascending aorta thus splits into two limbs which join to form the descending aorta. Between the two limbs lay the esophagus and trachea or only the latter. There are two types.

A. Partially obliterated double aortic arch.—The anterior or left arch persists as a cord, whereas the posterior one or right arch carries the blood.

B. Completely patent double aortic arch.—Both the anterior and posterior limbs are patent. Usually the posterior one is much the larger. This anomaly may produce pressure on the trachea or esophagus or both and there may result dysphagia; stridor may occur and persist. Barium meal may show esophageal pressure; the air shadow in the trachea may show deformity, or Lipiodol may be used as a spray or instilled with the bronchoscope to visualize the trachea. If symptoms are severe, surgical relief may be instituted. The posterior and usually the larger arch cannot be attacked surgically. The anterior (left) and usually the smaller may be divided between ligatures and other anomalous vessels moved aside and held in place with sutures through the adventitia of these vessels and sutured to the chest wall (Gross).

III. *Anomalous Right Subclavian Artery.*—Arises from the left side of a normal aortic arch and crosses the midline, compressing the esophagus from behind, then coming to a normal exit from the right thoracic cage. It may also run in front of the trachea or between the trachea and esophagus. Rarely this anomaly gives rise to dysphagia or respiratory distress. The dysphagia has been called dysphagia lusoria (Bayford) from *lusus naturae* (a freak of nature). Surgery may provide relief by a division of the offending subclavian. Due to the good collateral circulation which communicates with the second and third part of the subclavian and with the axillary artery, the first part of the subclavian may be divided without impairment of circulation to the arm.

IV. *Patent Ductus Arteriosus.*—During fetal life the ductus forms a by pass from the pulmonary artery to the aorta, thus avoiding the inactive lungs. Normally the ductus closes during the neonatal period (first two weeks of life) but sometimes it remains patent (about 1 per cent after the first year of life). Should this anomaly persist, blood is shunted from the aorta into the pulmonary artery. Depending on the size of the ductus, 45 to 75 per cent of the blood pumped by the left ventricle is shunted. Since this blood has just been through the

lungs for oxygenation and has returned to the left auricle by the pulmonary veins, this is a useless circuit. That portion of the blood in the aorta which is not shunted goes to the rest of the body and is returned to the right atrium by the venae cavae; from here, to the right ventricle. Thus the right ventricle has only one source of blood (that is, the peripheral circulation), whereas the

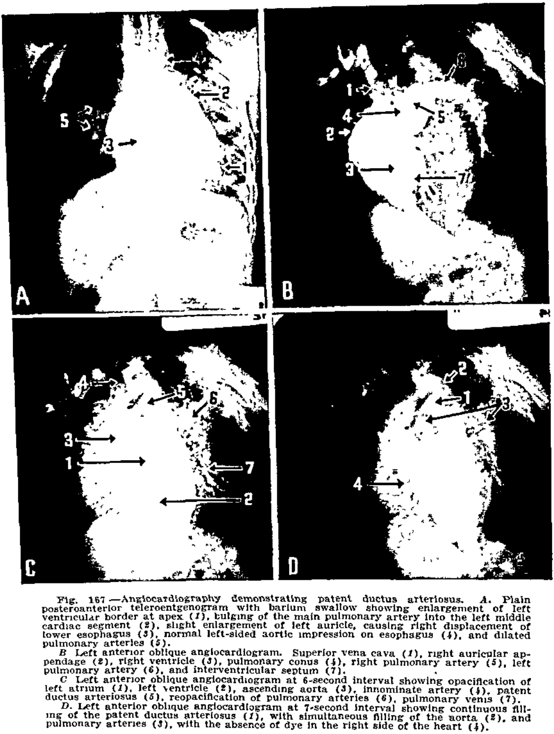

Fig. 167.—Angiocardiography demonstrating patent ductus arteriosus. *A*. Plain posteroanterior teleroentgenogram with barium swallow showing enlargement of left ventricular border at apex (*1*), bulging of the main pulmonary artery into the left middle cardiac segment (*2*), slight enlargement of left auricle, causing right displacement of lower esophagus (*3*), normal left-sided aortic impression on esophagus (*4*), and dilated pulmonary arteries (*5*).

B. Left anterior oblique angiocardiogram. Superior vena cava (*1*), right auricular appendage (*2*), right ventricle (*3*), pulmonary conus (*4*), right pulmonary artery (*5*), left pulmonary artery (*6*), and interventricular septum (*7*).

C. Left anterior oblique angiocardiogram at 6-second interval showing opacification of left atrium (*1*), left ventricle (*2*), ascending aorta (*3*), innominate artery (*4*), patent ductus arteriosus (*5*), reopacification of pulmonary arteries (*6*), pulmonary veins (*7*).

D. Left anterior oblique angiocardiogram at 7-second interval showing continuous filling of the patent ductus arteriosus (*1*), with simultaneous filling of the aorta (*2*), and pulmonary arteries (*3*), with the absence of dye in the right side of the heart (*4*).

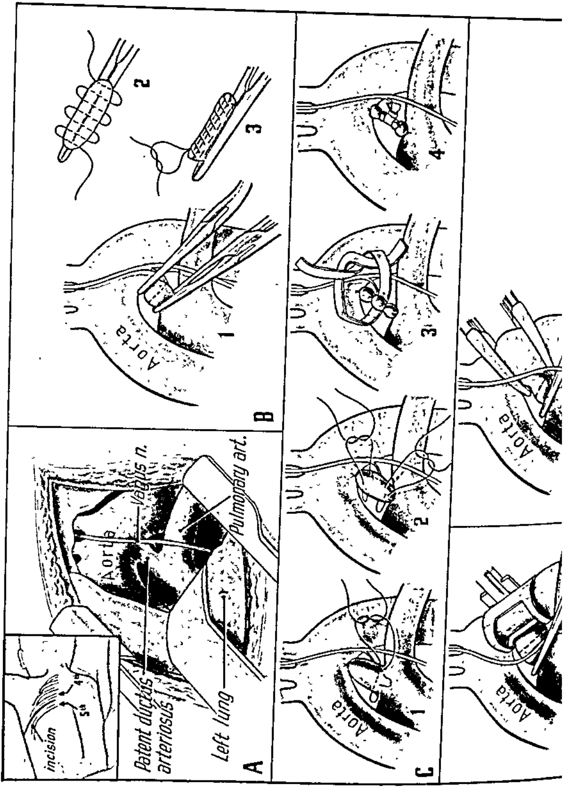
A
incision
4th
5th
Patent ductus arteriosus
Left lung
Aorta
Vagus n.
Pulmonary art.
B
Aorta
1
2
3
C
Aorta
1
2
3
4
Aorta
Aorta

Fig. 168.—Patent ductus arteriosus Diagrams illustrating methods of treatment for patent ductus arteriosus. In all methods the greatest hazard is the possibility of tearing the ductus at its juncture with the aorta. The fibrosis of the ductus, together with the possibility of a subacute bacterial endarteritis, makes this a vulnerable site for tearing. The best approach is an exposure through a posterolateral incision over the fourth rib and resection of the left fourth rib or incision in the fourth intercostal space without rib resection. This gives adequate exposure and enables the surgeon to take care of any possible exigency. The ductus was first ligated by Gross with various types of suture material and then after there had been several recurrences or recanalizations, larger suture material and cellophane were wrapped around the ductus. Finally the ductus was divided and both ends sutured. This, of course, is the best way in which to be sure that recurrence or recanalization will not occur. The various methods are illustrated. *A*. The surgical approach to the ductus and important anatomical structures surrounding it. Note that the recurrent laryngeal nerve lies immediately beneath the ductus. *B*. The treatment of patent ductus as outlined by Potts using his new clamps which are straight and angulated and which will not slip or injure the vessel wall. (*1*) The ductus is divided and, (*2*) continuous mattress suture of 00000 silk is introduced. (*3*) The end is then sutured with a continuous over-and-over stitch. *C*. A method advocated by Blalock in which a purse-string suture is placed about the ductus on the aortic and on the pulmonary side (*1*). Then two mattress sutures are placed between the two purse-string sutures (*2*), and finally umbilical tape is placed around the ductus (*3*) and tied (*4*). *D*. A method advocated by Jones using the Potts aortic clamp after mobilization of the aorta and the Potts ductus clamp or any other covered hemostat on the pulmonary artery side of the ductus and dividing between the two ends, both of which are sutured. The advantage of this method is that should the ductus be torn in efforts to free it, the Potts clamp on the aorta would prevent hemorrhage from this vessel and would, at the same time, not occlude it. Complete occlusion of the aorta may produce a paraplegia within twenty-five to thirty minutes in experimental animals due to anoxemia of the spinal cord cells. *E*. The Crafoord technique consists of placing shod clamps across the aorta, one above and one below the ductus, and a third on the ductus itself as close as possible to the pulmonary artery. The ductus is divided and the aortic side is sutured. The clamps are then removed from the aorta and the pulmonary artery side is sutured. Dr. Crafoord has not reported any paraplegias with this technique. This is explained on the basis of an adequate collateral circulation.

left ventricle has two sources (that is, the blood from the right ventricle and the blood returning from the short circuit through the pulmonary artery, pulmonary veins into the left atrium, and then the left ventricle.) The left ventricle must therefore pump from two to four times as much blood as the right. The leakage of blood from the aorta which has a higher pressure to the pulmonary artery which has a lower pressure results in a fall of diastolic pressure and a slight rise in the pulmonary artery pressure. There is usually a wide pulse pressure and upon exercise the diastolic pressure may drop to zero. As in other vascular fistulae, there is a compensatory increase in the total volume of circulating blood, both plasma and cells, but in large shunts this is inadequate to meet nutritive requirements.

If this abnormal communication is not large, no serious effects are noted and such individuals remain active. Complications may result from this malformation which may be serious. These are: (1) The shunt may divert so much blood from the peripheral circulation that the physical growth is retarded and the individual stunted. (2) The leak may be so great that the useless passing of blood through it may greatly increase the work of the heart, reducing cardiac reserve even to the point of cardiac failure. (3) Endarteritis of the pulmonary artery or *Streptococcus viridans* endocarditis may be superimposed. (4) Other complications such as aneurysmal dilatation of the ductus, rupture of the ductus, and embolism from thrombosis of the ductus may occur.

The diagnosis may be difficult up to the fourth year of life. After this, the physical manifestations are typical. These are (1) "machinery murmur" which is continuous but is accentuated during systole, maximum loudness in the second or third interspace to the left of the sternum, (2) thrill in the pulmonary area, (3) stunting of growth, (4) absence of cyanosis and clubbing of fingers, (5) history of heart disease from early childhood. Fluoroscopic and x-ray examination show (1) enlarged pulsating pulmonary vessels, (2) enlarged heart, (3) enlarged pulmonary artery, (4) pulmonary congestion. The electrocardiogram is normal.

The treatment of this anomaly is its surgical interruption. Although not all authorities are agreed on the indications for surgery, most believe that it should be ligated if the patient can stand the procedure. Simple ligation may not be curative due to recanalization. Ligation with Polythene wrapped around the ductus, purse-string ligation, double ligation with injection of sclerosing agent between ligatures, and ligation with division have been used. Division of the ductus precludes recanalization and is the treatment of choice. The mediastinal pleura is incised medial to the vagus nerve. A small amount of the pericardial sac may have to be separated from the ductus. The posterior portion of the ductus must be dissected from the bronchus blindly. The line of cleavage is through the adventitia. By using special Potts clamps, even a short ductus may be divided and the ends sutured. However, this is possible only if the ductus is long enough. If ligatures are tied too loosely, tiny crevices are left due to the wrinkled and folded walls; this invites recanalization; if too tight, the ligature may cut through with re-establishment of the lumen or the development of hematoma or fatal hemorrhage. If division between ligatues or sutures is not feasible, simple ligation and in addition a purse string may prevent its reformation. Results have been gratifying.

V. *Coarctation of the Aorta.*—Coarctation of the aorta is a narrowing or obstruction to the flow of blood in the thoracic (usually) or abdominal (rarely) aorta. It is said to occur about once in every 1,500 autopsies, most often in the distal part of the arch or beginning of the descending aorta near the ductus arteriosus or the ligamentum arteriosum. If the obstruction is due to a diffuse narrowing or atresia proximal to the origin of the left subclavian, there may

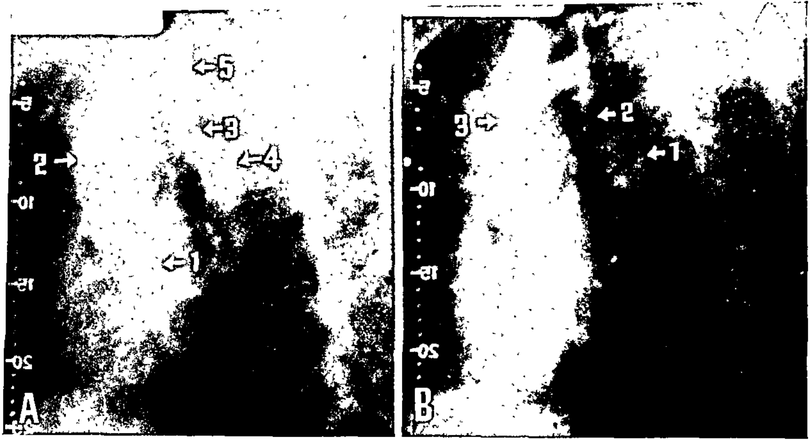

Fig. 169.—*A*. Angiocardiograms showing coarctation of the aorta. Left anterior oblique angiocardiogram at eight seconds after 70 per cent Diodrast injection showing left ventricle (*1*), ascending aorta (*2*), coarctation of aorta (*3*), poststenotic dilatation of aorta (*4*), left subclavian artery (*5*). *B*. Left anterior oblique angiocardiogram at 9 seconds showing poststenotic dilation of aorta (*1*), coarcted area (*2*), and aortic arch (*3*).

be an insufficient supply of blood to the arm, and if the site or origin of the left common carotid is involved, there may also be a deficient blood supply to the brain. Moreover, in this high obstruction there is more apt to be associated cardiac malformation which may lead to a fatality in the first few months of life (infantile type). In the so-called adult type the stenosis is limited to a short segment beyond the origin of the left subclavian in the region of the ductus arteriosus or ligamentum arteriosum.

The complications which may ensue are (1) atheromatous changes and thrombosis, (2) rupture of the aorta due to its sclerosis and increased strain, (3) aneurysm of a localized or dissecting type proximal or distal to the narrowing, or both, (4) superimposed infection with *Streptococcus Viridans*, endarteritis, or endocarditis, (5) elevation of blood pressure in the upper part of the body due to the direct result of mechanical blocking in the main arterial pathway. As a result of this elevation of pressure in the upper part of the body there may be (a) no bad effects over long periods, (b) cardiac failure, (c) central nervous system hemorrhage. Patients usually die between the ages of 16 and 30 years. (6) Due to the prolonged ischemia of the kidneys certain changes occur in them which are thought to be related to the pressor mechanisms causing hypertension. It is a fact that even after surgical excision of the coarctation with restoration of normal continuity there may remain a persistent progressive hypertension.

The diagnosis is made by: (1) Studying the differences in pressure of the arms and legs. Normally the systolic pressure is 20 to 40 mm. of mercury higher in the legs than in the arms. In coarctation this is reversed and the pressure in the lower extremities may be unobtainable with the sphygmomanometer. There is a decreased pulse volume in the lower extremities often associated with numbness and coldness. If the presure in the arms is normal and not elevated, the narrowing may be minimal or good collateral circulation may be present. Differences of pressure in the two arms greater than 30 to 40 mm. of mercury suggest that the aorta is blocked proximal to the subclavian. In children, pressures in the arms are not greatly elevated. (2) Abnormal pulsations. These can be seen or felt (in thin persons) in the intercostals and around the axillary and scapular arteries. Collateral circulation forms in direct proportion to the degree of obstruction. (3) Systolic murmurs. These may be due to the coarctation, but murmurs are unreliable as they may be due to associated cardiac defects (bicuspid aortic valve, patent interventricular septum, patent ductus arteriosus); large tortuous collaterals may also give rise to a murmur. (4) X-ray findings. These consist of cardiac enlargement and beyond the first decade of life the following evidence: (a) Cardiac hypertrophy and dilatation are pronounced where there has been long-continued hypertension. (b) The aortic knob is usually small and lacks its normal prominence. (c) Aortic indentation may be seen. (d) There is notching or scalloping along the inferior edges of the posterolateral portions of the ribs due to erosion by pulsating tortuous intercostal arteries; this is seldom present in the upper and lower two ribs. (e) Direct demonstration by angiocardiography or aortography. (5) Ballistocardiograms show a shortened J. K. stroke. In the normal there is a full and uninterrupted downward J. K. stroke which represents the decelerated impact of ejected blood as it strikes the major peripheral resistance. The shortened stroke is due to the abrupt and early interruption of the flow.

Surgery is the only available means of combating the effects of the anomaly. The objections to the early attempts at surgery were as follows: (a) Clamping of the upper thoracic aorta in dogs was followed by spinal cord degeneration and paralysis of hindlimbs. This was due to the fact that there were not collaterals and the time consumed in anastomosis was too long (over

FIG. 170.—*A*. Plain posteroanterior teleroentgenogram showing right aortic arch causing impression on right side of barium column in esophagus (*1*), absent pulmonary artery shadow (*2*), large long aortic arch (*3*), dilatation of left ventricle (*4*), and enlarged bronchial arteries (*5*).

B. Left anterior oblique angiocardiogram at 1½ second interval. Right auricle (*1*), right ventricle (*2*), dye spilling into left ventricle through high interventricular septal defect (*3*), opacification of aorta (*4*), absent pulmonary artery (*5*).

C Left anterior oblique angiocardiogram at 2-second interval. Right-sided aorta, descending on right side of spine (*1*), right ventricle (*2*), left ventricle (*3*), bronchial arteries arising from aorta (*4*).

D Left anterior oblique angiocardiogram at 5-second interval showing extent of bronchial arterial circulation (*1*), conspicuous loss of opacification of pulmonary veins and left atrium (*2*).

forty-five minutes, but it may occur in twenty minutes due to anoxemia, persistent vasospasm, or other factors as yet not determined). (b) Hemorrhage from the suture line. (c) Thrombosis. (d) Readjustment to the decreased resistance after the anastomosis. Crafoord and Nylin, Gross, Potts, Blalock, and others were the first to report successful resections and anastomoses without any untoward effects. Anticoagulants are unnecessary. Prior to this time extensive thoracic sympathectomy was done, but this resulted in only temporary improvement. Alexander was the first to ligate above and below the aneurysm and coarctation and resect them; collateral circulation was sufficient to result in a successful outcome, although the patient died later of cerebral hemorrhage. Blalock and Park suggested by-passing the coarctation by anastomosing the left subclavian with the aorta; this was tried in animals with success and has been used in man also, when the area involved in the coarctation is too long to permit resection and end-to-end anastomosis.

At present, Gross, Bill, and Peirce are using preserved arterial grafts for such cases, securing specimens from human subjects who have died in auto accidents.

Various clamps are used to hold the cut ends. The ingenious Potts clamp with its row of very fine teeth in the opposing jaws does not injure the artery and does not slip provided the clamp is applied to the vessel and not to intervening tissue. The principle is that of the Indian fakir who walks on spikes because he steps on many points at the same time. We have used small intestinal clamps shod with hollow shoestring. These do not slip and do not injure the arterial wall as proved in experimental animals. The ends of the aorta are sutured with interrupted or continuous everting mattress sutures, using No. 0000 silk swaged on No. 9 curved needle (Deknatel). Over and over suture is also successful and is easier to place. Interrupted everting sutures are less apt to be followed by lack of growth as the aorta grows.

Fig. 168*a* illustrates these abnormalities.

SYMPTOMS AND SIGNS AND TREATMENT OF PRESSURE-PRODUCING ANOMALIES

No doubt many individuals go through a normal life without symptoms from these anomalies. There may be dysphagia, stridor, dyspnea, cyanosis, hoarseness, cough, pain in the upper chest and arms. The outline includes the chief diagnostic features and complications. It is by a combination of symptoms and physical signs, together with careful fluoroscopic and x-ray examination, including barium meal studies of the esophagus, that the diagnosis can be made. Many times the true condition is not recognized until the chest has been explored. The treatment consists of ligation and division of the "offending" vessel wherever feasible. These maneuvers are shown in Fig. 166. It is important to note that the large vessels may be ligated, divided, and transplanted in children with anomalies due to the enormous collateral circulation. The carotid is the only exception and this not often in children.

Postnatal Cardiac Disease and Defects That Are Amenable to Surgery

1. Sudden Heart Failure.—Sudden heart failure during surgery may occur as a result of undue stimulation of the vagus nerves, handling of the heart, nerve shock, or causes unknown. It may be encountered

during any operation but is seen principally in (1) operations on the heart and pericardium (traction or pressure or handling of the heart may cause extrasystoles, ventricular fibrillation, and auricular *fibrillation*); (2) in any operations within the chest such as lobectomy, pneumonectomy, removal of mediastinal tumors, esophagectomy; (c) in operations of the upper abdomen or elsewhere; (d) in electrical shock.

Remedies and prophylactic measures which may be instituted may be divided into two large groups; namely, those which prevent or correct anoxemia (anoxic, anemic, stagnant, or combinations) and those which restore the heartbeat (ventricular standstill or asystole and ventricular fibrillation): (1) In surgery on the heart or pericardium, fibrillation may develop due to excessive stimulation of the vagus nerves or from handling of the heart. Beck and co-workers have recommended the use of 2 per cent procaine over the heart to desensitize it, and should fibrillation occur, 2 c.c. of a 5 per cent solution of procaine in 10 c.c. of physiological solution of sodium chloride may be injected into the right ventricular cavity. If then the heart stops, 5 to 10 c.c. of a 1 per cent solution of calcium chloride may be injected int the right ventricular cavity and may be repeated. A 0.1 per cent procaine solution of physiological saline is given intravenously as a slow drip during cardiac surgery routinely by many surgeons. (2) In pneumonectomy the hilus of the lung is injected with procaine or Metycaine before it is severed. The same is true in lobectomy. In addition, the small dissection sponges are soaked in a 1 per cent Metycaine solution. In case of ventricular fibrillation, restoration of the coordinated beat is impossible until fibrillation ceases. In all chest operations cardiac massage by manually squeezing the ventricle is useful when the heart stops. The pericardium may be opened and by gently squeezing every second, an artificial systole may be obtained. This, together with artificial respiration (by the endotracheal closed system in chest surgery), may oxygenate and circulate the blood and prevent death and injury to brain cells and heart muscle cells. (3) In any operation or circumstance where cardiac standstill occurs, Adrenalin, 1 c.c. of a 1:1,000 solution, may be injected into the right atrial chamber—the atrium rather than the ventricle because the needle puncture may set up fibrillation, and ventricular fibrillation is more difficult to control. The right atrium may be hit by going into the third or fourth interspace just to the right of the sternum. If no Adrenalin is available, a quick thump over the precordium or the insertion of the needle momentarily into the atrium may restore the beat. In abdominal operations the heart may be massaged through the diaphragm, or an abdominal incision high in the epigastrium may be made expressly for this purpose. A dilated heart or one which is greatly hypertrophied or the seat of advanced coronary disease cannot be resuscitated but any or all of the mentioned measures may be tried. The occasion for resuscitation is not common and its success is meager. We have succeeded on one occasion. The operation was our

first transthoracic esophagectomy in the human being. It was done for a carcinoma of the lower third of the esophagus. The upper third of the stomach had been removed and its proximal end closed. The posterior row of sutures had been placed, anchoring the esophagus to the anterior wall of the stomach, and the incision in the stomach had been made preparatory to completion of the anastomosis. At this time the heart stopped. Adrenalin, 1 c.c. of a 1:1,000 solution, was injected into the right ventricle and the ventricle gently massaged; 10 mg. of procaine hydrochloride was injected into the intravenous tube. Soon the heart began beating again. The operation was completed and the man made a smooth recovery. Summary: When the heart stops during an operation, the following measures should be instituted at once: (1) artificial respiration and oxygen. This prevents anoxemia and mechanically helps propel blood through the pulmonary circulation (Chapter 19). (2) Cardiac massage. With the patient in slight Trendelenburg position the heart may be massaged at the rate of 40 to 50 times per minute. This may stimulate contractions, and in addition it helps propel blood while the heart is regaining its ability to contract. This measure is easy enough in chest surgery. In other varieties the chest should be opened at once if an endotracheal tube is in place. If not, massage through the diaphragm should be started. Later, after the endotracheal tube is in, the diaphragm may be opened and cardiac massage continued. (3) Blood volume must be restored by blood and fluids. (4) Procaine hydrochloride, 50 to 60 mg. at a time in adults, should be given intravenously. (5) Two per cent procaine solution injected into the pericardial cavity about 5 c.c. at a time. (6) Five per cent procaine into the right atrium or right ventricle. (7) Adrenalin, 1 c.c. of 1:1,000 solution, injected into the intravenous tubing is useful particularly to increase arteriolar tone.

2. **Tamponade.**—If the heart action is impaired by fluid (blood or pus), *cardiac tamponade* occurs. This, of course, interferes first with the venous return. Should the intrapericardial pressure equal the systolic pressure, heart action would be impossible. As a result of the tamponade, which obviously first affects venous pressure, there is widespread edema, which first manifests itself by effusions into the pleural and peritoneal cavities. Lastly, there is general anasarca.

The chief symptoms will be a rising venous pressure with distention of the neck and arm veins, even though the arms are elevated, a falling arterial pressure with cyanosis, and faint and rapid heart sounds. In addition, the pulse is weak, often pulsus paradoxus (a pulse that is weaker during inspiration) and the skin is cold and clammy.

The causes of cardiac tamponade are penetrating wounds of the heart and great vessels, with extravasation of blood into the pericardial cavity, rupture of a myocardial infarct or aortic aneurysm, nonpenetrating wounds causing a contusion to the heart with rupture; rapidly developing effusions

or exudations or gas (pneumopericardium) in the pericardium will produce the clinical picture described. As in other instances of compression (meninges, pleura, peritoneum), the speed of its development determines the degree of symptoms. Electrocardiographic changes in the T waves and RS-T segments may occur. The *treatment* will depend upon the cause, but pressure should always be released by pericardial aspiration or by opening the pericardium (pericardiotomy). In heart injury from penetrating or perforating wounds, pericardial aspiration should be done at once and blood volume restored. If the leak is small, one or two aspirations may be sufficient, and no further surgery may be necessary. Should the pericardium fill up again rapidly, then the treatment of the primary cause is mandatory; that is, suture of the wound in the heart. Since the time element is of great importance, we usually aspirate and prepare for surgery at once, not waiting for reformation of tamponade. Pericardiotomy may be indicated in hemopericardium, suppurative and constrictive pericarditis, foreign bodies, and neoplasms. Tamponade may be absent in wounds of the heart if the pericardium is widely torn. Early shock and hemothorax are present very early.

3. **Infections and Inflammations of the Pericardium.**—As in infections elsewhere, the pericardium may be acutely inflamed, giving rise to various types of exudates, or it may be involved in a chronic cicatrizing process. The *acute* varieties have been classified according to their exudates as fibrinous, serofibrinous, serous, and purulent. The predisposing causes are pneumonia, acute rheumatic fever, empyema, wounds of the pericardium or heart, lung abscess, septicopyemias from any source. The causative organisms may be streptococci, staphylococci, pneumococci, meningococci, gonococci, *Bacillus coli,* the influenza bacillus. The disease is rarely primary, and, in addition to the pathological states mentioned, pericarditis is sometimes found in association with chronic nephritis with uremia, coronary thrombosis, and myocardial infarction, rarely with the acute exanthemas.

The symptoms and signs are those of the primary condition plus the heart effects. Often the diagnosis is missed. The symptoms and signs of infections include chills, sweats, fever, rapid pulse, malaise, anorexia, leucocytosis, and rapid wasting; in addition, substernal pain, dyspnea, dysphagia, enlarged neck veins, and all of the other symptoms of cardiac tamponade; in the dry form a friction rub may be heard, increased cardiac dullness on percussion, and, if effusion is present, distant heart sounds on auscultation, dimunition of cardiac movement on fluoroscopic or kymographic examination; x-ray studies may show obliteration of cardiophrenic angles.

Diagnosis depends on the symptoms and signs and exploratory incision (pericardiotomy) or aspiration (pericardicentesis). The latter is not without danger, for the coronary vessels, heart, or lungs may be injured. The best site for diagnostic aspiration is in the sixth inter-

space just to the left of the sternum—here the internal mammary artery is more lateral to the sternum, as is also the pleura. Open drainage is indicated in purulent pericarditis and is preferable to repeated aspiration or aspiration with injection of penicillin because of the danger of injuring the heart. This is accomplished by subperiosteal resection of the fifth and sixth left costal cartilages for about 1 to 1½ inches. The pericardium is identified and the pleura avoided; a small aspiration needle is introduced. A sample of the exudate is sent to the laboratory for culture. If the exudate is serous or serosanguineous, penicillin, 200,000 to 500,000 units, may be introduced and the wound left open. If the exudate is purulent or if purulent particles are present, the pericardium is opened and its edges sewed to the muscles or fasciae. Penicillin is instilled into the pericardial sac and is given intramuscularly in doses of 300,000 units every three hours. Sulfonamides are also given by mouth. Rarer types of infection as revealed by culture may require streptomycin, aureomycin, or Chloromycetin.

4. **Chronic Adhesive Pericardial Disease** (Adhesive Pericarditis; Adherent Pericardium; Chronic constrictive pericarditis; Pick's Disease; Pericardial Scar; Concretio Cordis; Accretio Cordis).—Scar tissue may limit the function of an organ due to a mechanical interference with its motion. This is true of dense adhesions about the lungs and intestines as well as the heart. In the latter instance the fibrous adhesions form between the epicardium and myocardium (intrapericardial), partially or completely obliterating the pericardial space (concretio cordis). Less often fibrous adhesions extend from the pericardium to the pleurae, diaphragm, chest wall, the hila of the lungs, and mediastinal tissues (extrapericardial), also interfering with function (accretio cordis or mediastinopericarditis). The *cause* of this condition is usually an antecedent acute pericarditis. Sometimes it is due to the tubercle bacillus or the pneumococcus, rarely to mediastinitis, or no recognizable cause for the calcified pericardium may be found. Rheumatic fever is probably more often the cause of mediastinopericarditis.

Pathology and Disturbed Physiology.—Normally the pericardium is attached to the posterior aspect of the sternum and the diaphragm by fascial bands and the roots of the lungs (through the pulmonary vessels). Since the lung roots are movable during respiration and the bands are loose, the heart may move and swing with respiration unimpeded. Should external adhesions occur to the lung root or other structures, movement would be curtailed or actual rotation or torsion may take place so that blood cannot adequately enter or leave the heart. Such conditions permit the heart to struggle against its "leashes," causing cardiac hypertrophy (especially if there is a complicating hypertension or valvular disease). There may be great thickening of the pericardium encasing the heart with scar tissue, or calcium may be deposited within this scar—even bone has been found here. The heart is compressed; hypertrophy cannot occur

even if there are external adhesions or valvular disease. Blood cannot enter the heart in diastole, and venous pressure rises. Since liver veins have no valves, there is an early hepatic enlargement due to passive congestion; also no valves are present in the intraabdominal veins (except azygos and spermatic or ovarian) or the intrathoracic veins, so ascites and pleural effusions occur in that order. Unlike myocardial failure, the edema in the extremities follows the above and does not precede it, although there is edema on exercising, early in the disease. Late there is generalized

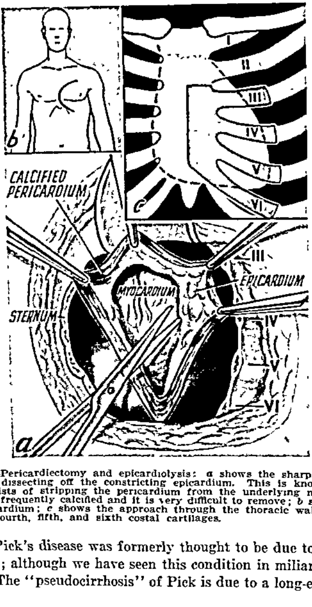

Fig. 171a.—Pericardiectomy and epicardiolysis: *a* shows the sharp dissection which is required in dissecting off the constricting epicardium. This is known as epicardiolysis and consists of stripping the pericardium from the underlying myocardium. The pericardium is frequently calcified and it is very difficult to remove; *b* shows the incision over the pericardium; *c* shows the approach through the thoracic wall with resections of the third, fourth, fifth, and sixth costal cartilages.

anasarca. Pick's disease was formerly thought to be due to a tuberculous polyserositis; although we have seen this condition in miliary tuberculosis, it is rare. The "pseudocirrhosis" of Pick is due to a long-existing passive congestion.

Symptoms and Signs.—Usually the diagnosis is not difficult. The two most common conditions which simulate the disease are cirrhosis of the liver and arteriosclerotic disease with congestive heart failure. The

symptoms which are noted first are general weakness and fatigue, dyspnea, digestive disturbances, and later swelling in the abdomen and last in the extremities. The chief signs are a "small silent" heart, liver enlargement, ascites, pleural effusion, general edema, congestion of neck veins and later all veins, pulsus paradoxus, low blood and pulse pressure, and high venous pressure. Laboratory findings include elevated venous pressure and decreased circulation time. X-ray studies show a normal-sized or small heart, often with calcareous plaques. On fluoroscopic examination there is found a decrease in the amplitude of the pulsations, especially on the right border. Electrocardiogram, according to most observers, is helpful. Broadbent's sign (a tug on the tenth and eleventh intercostals) may be present.

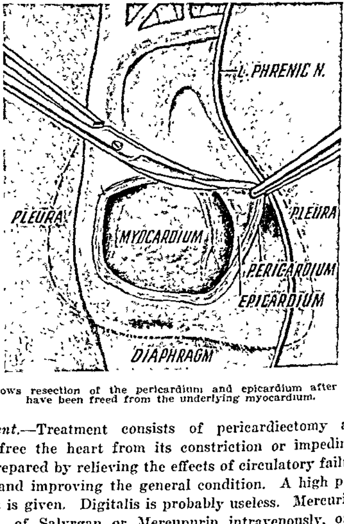

Fig. 171b.—Shows resection of the pericardium and epicardium after the structures have been freed from the underlying myocardium.

Treatment.—Treatment consists of pericardiectomy and epicardiolysis to free the heart from its constriction or impediments. The patient is prepared by relieving the effects of circulatory failure as much as possible and improving the general condition. A high protein, high vitamin diet is given. Digitalis is probably useless. Mercurial diuretics (1 to 3 c.c. of Salyrgan or Mercupurin intravenously, or Mercuhydrin or Thiomerin may be used) preoperatively and postoperatively are helpful. Transudates are withdrawn from the pleural and peritoneal cavities. A curved incision is made to the left of the sternum from the second to the sixth rib. The costal cartilages are divided

subperiostally. The internal mammary artery is ligated. The pleura is gently dissected loose from the pericardium to avoid injuring it. If densely attached, it is dissected loose after the pericardium has been removed because pneumothorax may make the operation hazardous. Incision of the pericardium is made over the left ventricle first—it has been said that freeing of the right ventricle first may cause pulmonary edema because blood would be pumped in large quantities to the lungs and the left atrium could not accept it. We have not noted this. The interventricular groove contains the descending branch of the left coronary, and particular care is exercised not to injure this. The separation of the epicardium from the myocardium is desirable and should be

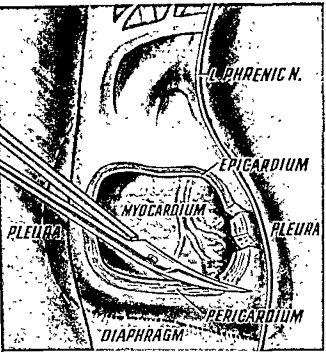

Fig. 171c.—Shows the method of multiple incisions into the margins of the remaining epicardium and pericardium (Modified from Harrington: Ann. Surg. 120: 468, 1944.)

done in addition to resection of a part of the epicardium and pericardium. In the course of the operation the pulse becomes rapid and sometimes irregular. The latter calls for temporary cessation of the operation. Moist sponges with physiological saline are applied to the heart; also procaine as previously described (see auricular fibrillation). The upper part of the wound is closed carefully, including the intercostal muscles to the sternum. The fifth and sixth cartilages are removed and this area is closed only by subcutaneous tissue and skin. Two Penrose drains are inserted in the lower angle to take care of serous exudate. They are removed in thirty-six to forty-eight hours. Oxygen is used postoperatively. The mortality of this operation is about 35 per cent.

5. **Cardiac Trauma.**—The heart may be injured with or without penetration as is the case in abdominal injuries (Chapter 20). Contusions and compressions of the chest are not uncommon in automobile accidents where the driver is thrown against the steering wheel. The heart may be slowed greatly by vagus nerve stimulation after chest contusions, its myocardium may be injured and inactivated by ecchymosis, or the heart may rupture. Doubtless the last effect is more often seen in old arteriosclerotic hearts. The effects of extreme slowing may resemble the carotid sinus syndrome and with various degrees of syncope. A contused myocardium will give all the symptoms and signs of cardiac insufficiency and should be treated as such. Rupture of the heart will show the signs of tamponade and will require cardiorrhaphy. Aspiration should be done first to see whether the rent is of sufficient size to require open operation.

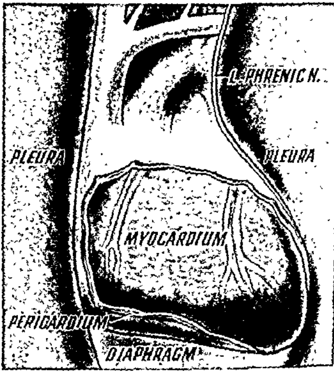

Fig. 171*d*.—The complete operation. Recent studies by Holman and Willett tend to prove that failures following pericardiectomy are due to incomplete decortication. This is chiefly due to adhesions about the superior and inferior vena cava. These authors believe that the exposure necessary for this type of decortication requires a median sternotomy with transverse division of the sternum in the second interspace. The diagnosis of constrictive pericarditis is based upon so-called Beck's triad which consists of the following symptoms: (1) a small, quiet heart; (2) ascites; and (3) increased venous pressure. The best proof that a complete operation has been done, which includes the liberation of all borders of the heart and both venae cavae and also the inferior cardiac border of the pericardium lying between the heart and the diaphragm, is a prompt and permanent lowering of the venous pressure.

Penetrating wounds of the heart are seen often in war but are by no means rare in civilian practice. The penetration may be very small when produced by small sharp instruments (ice pick). Sometimes foreign bodies will penetrate the pericardium and not enter the heart. More

often the wound is large enough to produce a hemopericardium with all of the symptoms and signs of acute tamponade as previously described. Thus a penetrating wound may produce very few symptoms or it may mimic various types of heart disease when foreign bodies are present, or it may cause serious interference with heart action due to tamponade. The diagnosis is not difficult with the aid of the x-ray and fluoroscope. In all cases of cardiac tamponade, progressive hemothorax, or persistent shock in chest injuries the possibility of a cardiac wound must be considered. The diagnostic signs as previously mentioned include a period of no symptoms following chest injury and then rapid collapse and shock, faint heart sounds and weak pulse, elevated venous pressure (normal being 6 to 12 cm. of water) as elicited quickly by holding the hands up and noting the persistence of distended veins, and, lastly, a low arterial pressure. These symptoms develop quickly because the pericardium is obliterated rapidly after the pericardium is distended.

Fig. 172.—This patient was a male, aged 45 years. He was stabbed with a large knife just to the left of the sternum in the third interspace. On admission the patient was pulseless, cold, and clammy. The blood pressure could not be obtained. The veins of the neck stood out prominently. The patient was gasping and was semi-conscious. A diagnosis of cardiac tamponade due to stab wound of the heart was made and the patient was explored through the third interspace. The third and fourth costal cartilages were divided and the ribs spread apart. The left pleural cavity was filled with blood due to the bleeding from the internal mammary artery which had been severed. This was doubly tied. The pericardium was opened and an enormous quantity of blood escaped. At this time the patient's blood pressure began to rise. Blood was aspirated from the pericardial sac but was collected in a sterile container and returned very rapidly in the antecubital vein and both anterior tibial veins. The rent in the right atrium was easily identified and was closed with interrupted sutures of silk. The pericardium was closed except for a very small opening which was left to permit egress of any accumulation of serum or blood in the pericardial sac. The pleura and intercostal muscles were closed with interrupted silk sutures. A catheter was placed in the suture line and suction was applied and the lung was inflated. The catheter was then withdrawn quickly and the sutures tied tightly. The costal cartilages were approximated with silk ligatures and the skin closed with interrupted silk sutures. *A*, Postoperative photograph showing the T incision which was made to gain adequate exposure. *B*, X-ray photograph of the patient on the fifth postoperative day. He made an uneventful recovery.

Pathology.—In general then there are three chief types of injury producing different clinical pictures and requiring different kinds of management: (1) The small perforating wound produces a small hole in the pericardium and in the heart. Bleeding is prodigious at first, but soon the hole is sealed due to the early clotting which in turn is caused by defibrination of escaped blood as a result of the cardiac action. For the same reason the hole in the parietal pericardium seals, causing early cardiac tamponade with its chain of symptoms and signs. (2) The large lacerated wound does not seal off in the heart or pericardium so that there is cardiac tamponade and signs of hemorrhage into the pleural cavity since blood cannot escape from the pericardium as rapidly as it is lost from the heart. (3) Incised wounds produce bleeding from the heart, and the pericardium is open so that the symptoms and signs are chiefly those of hemorrhage into the pleural cavity and to the outside. The defibrinated blood in all varieties remains liquid.

Usually the right ventricle is injured because of its vulnerable position; next, the left ventricle; then, the right atrium. Often there is associated injury to the pleura, lung, internal mammary artery, and, of course, the pericardium. Sometimes there are two or more holes present.

Treatment.—The treatment may be outlined as follows: Preoperative management consists of the administration of plasma and whole blood to restore blood pressure and encourage reaction from shock. Some authors advise against this because of the possibility of increasing the tamponade. Usually this is not true because blood is being lost rapidly through the pericardial rent, and, moreover, if the transfusion is not given under pressure, it will flow into the vein slowly due to the increased venous pressure. Most important is the fact that blood will be running into the cannulated vein in the ankle and arm when the pericardium is opened, and a large quantiy of blood is lost in a short time. Aspiration should be done first because it relieves tamponade, and in small rents caused by picks, pins, or small knives it may be curative (type 1). However, this should be done in the operating room while preparations are being made for immediate surgery (types 2 and 3). In a recent case of a large rent of the right atrium produced by a screw driver, over 2,500 c.c. of blood were lost and replaced in thirty-five minutes with complete and uneventful recovery after cardiorrhaphy. The anesthetic of choice is either administered by the endotracheal tube. Local anesthesia is undesirable and a waste of time—gas anesthetic agents may not be effective due to the severe anemia—ether is best. A T incision or a curved incision may be used. The second, third, and fourth costal cartilages are divided and the ribs spread, the internal mammary artery doubly ligated and divided, and the pleura entered through the third interspace. The lung is packed away and the pericardium opened. If the rent is immediately seen, the finger is held over it and it is sutured with silk. If manipulation is required,

5 c.c. of a 1 per cent procaine solution is injected into the right ventricular cavity to prevent severe bradycardia, asystole, or auricular fibrillation. Traction sutures in the ventricular apex are not usually employed. The pericardium is loosely closed so that serum may exude into the pleural cavity. The lung is inspected, then inflated, and the chest closed without drainage or with closed drainage if lung injury was present. Postoperative care consists of treatment for shock and its prevention by blood transfusion; anoxemia is treated by oxygen inhalation; penicillin and sulfadiazine are used to prevent infection. The patient is kept at rest for about three weeks.

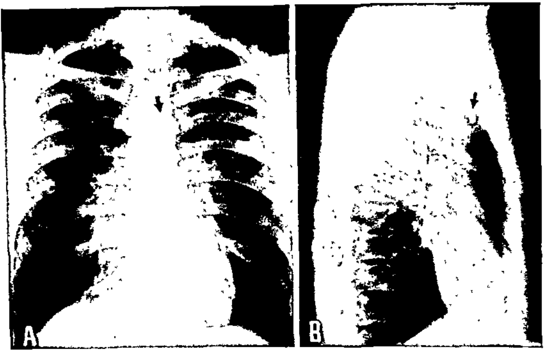

Fig. 173.—X-ray photograph showing a foreign body within the pericardial sac. This patient was a man 32 years of age, who complained of angina pectoris which had been diagnosed elsewhere. The pain was typical in its radiation and was not constant but came after the slightest exertion or excitement. The patient stated that when he was 12 years of age he was accidently shot in the chest and that the bullet had never been recovered *A*. Posteroanterior x-ray photograph showing the bullet to be directly over the ascending arch of the aorta and lying between the first and second ribs anteriorly. *B*. X-ray photograph in a left lateral view.

Operation was done through an incision which required the removal of the upper portion of the sternum and a portion of the first and second ribs. The bullet was found within the pericardial sac directly in the groove between the aorta and the pulmonary artery Following removal of this bullet the anginoid attacks disappeared and the patient has remained well. This is an illustration of some of the vagaries of the symptoms produced by foreign bodies within the pericardial sac. During World War II foreign bodies were found in all portions of the pericardial sac and the heart muscle as well, and some within the heart chamber. These were successfully removed in large numbers. This illustrates the problem as it appears in civilian practice. (Case referred by Dr. John MacDonald.)

Foreign bodies should be removed if severe symptoms occur (precordial pain, dyspnea, asthenia, and cardiac neurosis) or if there is evidence of pericardial or myocardial change or danger of a future complication such as dense fibrosis, infection, erosions of the myocardium

or vessel wall, embolism, and bacterial endocarditis. Since any of these complications may result, it is our policy to remove foreign bodies, except extremely small ones, early.

6. **Cardiac Ischemia.**—We have seen that the heart is permitted free motion by its anchorage to the body through the great vessels. This arrangement does not provide for continuity of tissue and therefore the development of new or compensatory vasculature does not occur readily. The superior, middle, and inferior cardiac nerves carry efferent fibers and are derived from the superior, middle, and inferior cervical sympathetic ganglia, respectively. In addition, there are some nerve fibers coming from the sympathetic ganglia of the second to the fifth thoracic vertebrae inclusive. These carry afferent and efferent fibers.

Ischemia of the heart muscle may be due to functional spasm of the coronary arteries or their occlusion. If it is the former, as may occur in angina pectoris, sympathetic ganglionectomy may help. If the latter, some method of forming collaterals is indicated.

Sympathectomy is done through a left paravertebral incision from the second to the sixth rib. Sometimes both sides must be interrupted; usually the left side is sufficient. Ribs are severed and spread apart. The pleura is pushed aside and the second to fifth dorsal ganglia and rami communicantes removed. The operation has some advocates and results are usually temporary.

If the coronary is occluded, collaterals must be established. Beck and colleagues have pointed out that the right coronary artery, the descending ramus of the left coronary artery, and the circumflex ramus of the left coronary artery possess capillary beds that do not anastomose with each other. Intercoronary communications may occur after occlusion provided death of the myocardium from infarction does not occur or ventricular fibrillation with heart failure does not ensue. The patient would perish from either. Since both are due to anoxemia, any method of delivering oxygenated blood would tide the patient over this critical period and then collaterals would form. Anastomoses also occur from inflammation—in fact, ligation of the coronaries may be done with survival of the experimental animal if abrasion of the heart had previously been carried out. A third method of stimulating collaterals advocated by Fauteux follows the idea used in peripheral vascular disease of stimulating collaterals by venous ligation—in the heart the vena magna cordis may be ligated in occlusion of the left ramus descendens of the left coronary. Beck has sutured parietal pericardium, mediastinal or omental fat, and skeletal muscle to aid in relieving myocardial ischemia. His results have been encouraging. The use of calcium and magnesium silicate in powder form used sparingly to produce irritation and collateral blood supply also has given promising results. Other substances used are talc, asbestos, and acriflavine. Admittedly these procedures are still in the experimental stage.

Other potential sources of new blood supply which have been utilized are the thoracic wall, including the pectoral muscles, the internal mammary and intercostal arteries, the pericardium and its fat, and the lung (cardiopneumonopexy—Carter).

Beck has recently succeeded in anastomosing the aorta to the coronary sinus using a transplanted vessel. He first ligates the coronary sinus so that it will enlarge and hypertrophy; then at a second stage the transplant (jugular vein, bronchial artery) is implanted. He has recently reported a successful case in a man using a portion of the bronchial artery as a graft.

Fauteux has attempted to relieve anginal pain by pericoronary neurectomy combined with ligation of the coronary sinus to increase the amount of blood available to the myocardium.

Aneurysm of the heart following severe contusion or following infarction may someday be treated by excision and suture as demonstrated by Murray, who successfully resected acutely infarcted areas in dog hearts.

7. **Valvular Disease.**—Stenotic valves have been dilated and incised, excrescences have been removed from valves in subacute bacterial endocarditis, and the human heart has been cannulated through the antecubital vein in the arm to help in diagnosis and treatment of cardiac disease. The results of intracardiac surgery are equivocal and the procedures are as yet experimental. Recently a new method has been advocated in the treatment of mitral stenosis so that the heart itself will not have to be attacked. This is proposed by Bland and Sweet. The operation consists of providing a venous shunt in advanced mitral stenosis so that blood is directed from the pulmonary vein into the azygos vein in order that the high pressure within the former will be decreased by shunting blood into the systemic venous system. The object of this operation is, of course, not to cure the mitral stenosis but to prevent the recurrent attacks of pulmonary edema which may be fatal and which are often encountered in advanced mitral stenotic disease. Other procedures designed to relieve the so-called "cardiac lung" due to left ventricular failure or mitral stenosis are ligation of the inferior vena cava below the renal veins to decrease the amount of blood reaching the right atrium and tricuspid valvulotomy which is also designed to delimit the volume of blood reaching the lungs.

Valvulotomy has been successfully performed by Bailey and others in mitral stenosis. The operation is performed without dislocating the heart from a position of optimum function. A small opening is made in the left auricular appendage or the left superior pulmonary vein and the cardiovalvulotome introduced. By this approach from the auricular side the funnel directs the cutting instrument toward the leaflet margin. A "selective insufficiency" is created and "valvuloplasty" by resection of the immobilizing commissure bridges. In this way mitral insufficiency is

not substituted for mitral stenosis. Undue acceleration of the heart increases pulmonary vascular pressure and is associated with attacks of pulmonary edema, and therefore tachycardia must be prevented if possible. Patients with mitral stenosis who have an adequate cardiac output but severe pulmonary symptoms either have a combined stenosis (insufficiency with the latter predominating) or the pressure in the left atrium may be extremely high so that an adequate flow may be maintained through the stenotic valve. In such cases perhaps the creation of an interatrial septal defect may relieve the pulmonary hypertension.

Rheumatic mitral stenosis is one of the most common causes for peripheral arterial embolism. The site of the thrombus from which the emboli originate is the left auricle or its appendix in most cases. Therefore, Madden has recently resected the left auricular appendix in patients with rheumatic heart disease and mitral stenosis with or without auricular fibrillation who have had peripheral arterial embolism.

Experimental Studies

Björck and Crafoord have shown that if oxygen is supplied to the brain, the rest of the body can do without it for twenty minutes or more without damage. Björck has described a cardiopulmonary machine which takes blood from the veins and lets it flow through a horizontal cylinder, the upper half of which is filled with a stream of warm oxygen flowing in the opposite direction. Discs rotating within the cylinder dip into the blood so that new films of blood are continually formed on their surfaces and oxygenated. The blood is returned by two pumps (working in parallel alternate pulsations) which are regulated by a photoelectric cell actuated by the blood level in the cylinders.

In order for the blood to flow without clotting, all surfaces are coated with silicones to make them smooth. To prevent embolism, the blood is passed through a fine-mesh filter, and to avoid hemolysis, oxygen is used and sodium bicarbonate solution is added to the blood. Lastly, to prevent hypoglycemia, glucose is added. The experiments have been done on dogs. The machine is filled with blood from a donor and this is pumped through the dog's external jugular vein into the superior vena cava and withdrawn from the common carotid, after traversing the lungs which have been automatically inflated by an automatic respiration machine. In this way the dog's brain is perfused with its own blood mixed with donor blood that has gone through its lungs. Experiments have shown that after the vertebral arteries and veins have been divided, the brain could be perfused through the right common carotid artery while the left one was clamped, venous blood being withdrawn from the superior vena cava by a cannula inserted through the external jugular vein. Dogs perfused in this way survived for ninety-three minutes and remained normal. Dogs survived thirty-three minutes with a superior and inferior venae cavae both occluded and azygos vein ligated. With this machine it is hoped that intracardiac operations can be performed by temporarily using an artificial heart as described.

Templeton and Gibbon have attempted intracardiac operations by doing their work in stages. First they found that dogs can tolerate clamping of both venae cavae for nine minutes without neurological damage. Their operations on dogs were done in stages as follows: Circulation through the heart was stopped for three minutes, resumed for the next forty-five, and stopped again for six minutes. The right auricle was incised and the right cusp and papillary muscle of the tricuspid valve resected. Then T-shaped vein grafts were fashioned from the azygos (to form a leaflet) carrying with them a stump of the supreme intercostal vein (to form the chorda tendinea). This

was turned inside out and the ends closed. Pericardium grafts were also trimmed to a T shape. Circulation was then interrupted long enough to permit a suturing of the graft in place.

Jongbloed has succeeded in constructing a mechanical heart-lung system which maintains the whole circulation to brain, spine, thoracic and abdominal viscera. Blood is pumped out from the superior and inferior vena cavae by way of the external jugular and femoral veins respectively; it is then oxygenated and pumped in (left heart of the apparatus) to both femorals, using a T tube, so that blood flows distally, and since the aorta is empty it flows proximally to the aortic valves which remain closed because there is no blood in the left ventricle and the artificial pressure in the aorta is higher than the pressure in the right ventricle. From the aorta blood flows normally to all aortic branches, including the coronaries. Animals have been kept alive for two hours with recovery with this apparatus.

8. **Cardiac Neoplasms.**—Cardiac neoplasms are extremely rare. In the pericardium, primary neoplasms, include fibroma, lipoma, angioma, and sarcoma. secondary tumors from the myocardium and mediastinum and bronchogenic carcinoma of the lung occur by primary extension or in the pericardial blood vessels. Echinococcus cysts have been reported in the pericardium.

Endocardial tumors that have been reported are as follows: vascular hamartoma, myxoma, fibromyxoma.

Myocardial growths are also very rare. Benign growths are as follows: fibroma, angioma, lipoma, leiomyoma, and myxoma. Rhabdomyoma is seen in connection with tuberous sclerosis (see Chapters 6 and 18). Sarcoma, primary and secondary, are reported. Melanoma may metastasize to the heart. Carcinoma from mediastinal structures (esophagus, lungs, thymus, lymph nodes), leucemia, and lymphosarcoma may involve the myocardium. Echinococcus cysts may be found in the heart.

Diagnosis is not so difficult now because of the help of angiocardiography, but the tumor is usually called a mediastinal tumor of lymph node origin. As exploratory thoracotomy becomes a more common operation many of these growths will be found. At least those of the pericardium may be amenable to surgery, and perhaps some of the epicardial and myocardial growths as well.

9. **Pulmonary Embolism.**—A discussion of the probable causes of this complication following surgery or bed rest will be *found in* Chapter 5 and also in this chapter under Veins. This ominous event strikes suddenly in young persons and old and often without warning. Some authors say that 16 per cent of postoperative deaths are due to pulmonary embolism. In 1936 we made a study of postoperative deaths in the Indiana University Medical Center for a period of five years. There were 5,133 so-called major operations with 155 deaths, a general mortality rate of 3 per cent. Of this group, 53, or about one-third of the deaths, were due to what we termed circulatory causes, an incidence of 1 per cent. These we divided into cardiac, arterial, venous, and hemorrhagic shock. Of the 53 deaths due to "circulatory" causes, 18 were due to pulmonary embolism. In 1940 we repeated our studies. There were

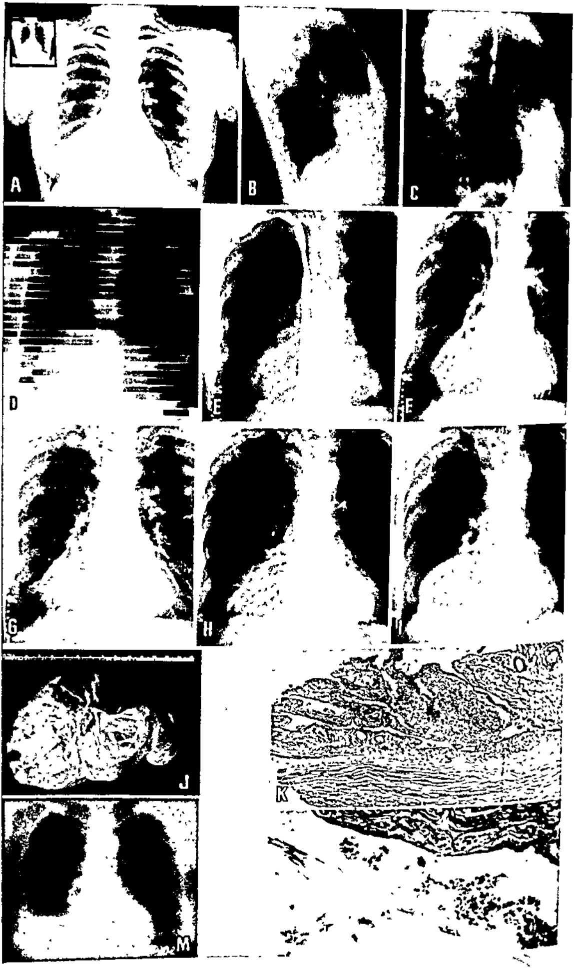

Fig. 174.—*See opposite page for legend.*

8,979 major operations with 162 deaths, a general mortality rate of 1.8 per cent. Of this group, 68, 42 per cent, of the deaths were due to circulatory causes, an incidence of 0.75 per cent. Of the 68, only 10 were due to pulmonary embolism.

The sudden collapse, pallor, cyanosis, dyspnea, and thready pulse, together with a sensation of a constriction about the chest, sometimes a cough or vomiting, and a fear of impending death, is the usual picture—not unlike coronary thrombosis. If there is a complete obstruction of the pulmonary artery, death will ensue at once. If the obstruction is incomplete, death may occur later due to diminished circulating blood volume and shock or to right-sided heart failure. (See Chapter 14.)

Death may occur in a few minutes; therefore, surgery must be prompt if embolectomy is to save life. Since the main pulmonary artery with a saddle embolus may be the cause, intrapericardial approach may be necessary. Trendelenburg described the operation. In 100 cases reviewed by Elkin, 15 are living. Since this per cent of survival is not much greater than that without surgery, the value of embolectomy is open to question. If the diagnosis can be made with certainty and surgery done immediately, the operation is indicated, followed by the use of heparin. Since this is ordinarily not feasible, more stress should be placed on the methods of prevention of pulmonary embolism, and its repetition in sublethal emboli, than on their cure. One last question still unanswered deserves consideration. Frequently an embolus in one pulmonary artery is lethal—why, then, is not pneumonectomy always fatal? Many hypotheses are given. A few of the more important ones are (1) the lung becomes acclimated to decreased blood supply in the interval

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Fig. 174.—Pericardial cyst (lymphogenous). Series of x-ray photographs and angiocardiograms which were necessary to work out the true nature of a mediastinal tumor and the removed specimen, microscopic picture of the specimen, and the postoperative x-ray photographs showing the lesion removed. (Lymphogenous cyst of the pericardium—cystic hygroma.) This woman, G. S., aged 57 years, had a routine chest film made by the State Board of Health Service and she was told that an abnormality existed and was referred to the family physician. The small x-ray photograph (inset in *A*) shows the routine 35 mm. film. X-ray photographs *A* and *B* show posteroanterior and lateral films of the chest. Following this procedure, we could not decide whether the lesion was a mediastinal tumor, an aneurysm of the right bentricle, a cyst of the pericardium, or a tumor of the ventricular wall. *C* is an x-ray photograph, lateral projection, showing a barium swallow which was made to rule out possible esophageal tumor. *D* is a roentgenkymogram which shows the tumor on the right side but does not aid materially in making a diagnosis between intracardiac or mediastinal tumor or pericardial tumor. Fluoroscopic examination was not helpful because of the transmitted pulsation. Angiocardiography revealed the diagnosis accurately. *E*. The first film taken shows the dye flowing into the right atrium. The small ball on the left shows the time in seconds. *F*. The dye is leaving the right ventricle and going into the pulmonary artery and its branches which are clearly seen in both lungs. *G*. The dye is now seen to be coming back through the pulmonary veins into the left atrium and the left ventricle. *H*. The dye is now seen in the left ventricle and is beginning to come out through the aorta. *I*. The aorta is now plainly visualized. It is to be noted that after the influx of dye into the right atrium and right ventricle, the diagnosis was clearly made because the tumor mass is seen to be outside of the heart. Since it was attached to the pericardium as noted by pulsation and since it was partially transluscent, it was diagnosed as a pericardial cyst *J* is a photograph of the removed specimen. *K* is a low-power photomicrograph establishing the diagnosis of a pericardial lymphatic cyst. The section shows some lymph spaces and small cystic spaces. *L* is a high-power photomicrograph. Note the endothelial lining, the lymphocytes, and smaller cystlike spaces which are probably dilated lymph vessels. The larger space is a large lymph vessel. *M* is the postoperative film taken in the posteroanterior position approximately ten days following extirpation of the cyst A very small amount of serum is present in the costophrenic angle. This was absorbed. The patient made an uneventful recovery and has remained well to date. (Case referred by Dr. Russell Henry.)

between thoracotomy and ligation; (2) arteries and veins are tied; (3) a wider area of artery is involved and the arterial spasm in both sides will be greater after embolism than ligation; (4) ligation under anesthesia and local *anesthesia at the hilus prevents auricular fibrillation.* (5) Small embolic particles lodge in the arterioles and capillaries of the lung in showers or in the arterioles alone. (6) A large embolus which is saddle in nature and occludes both main branches of the pulmonary artery.

10. **Mediastinal Emphysema.**—Mediastinal emphysema should be mentioned here because of its effect upon the heart. It is evident that if mediastinal pressure exceeds venous pressure, blood will not be returned by the veins to the right atrium and death from anoxemia will occur. The causes for mediastinal emphysema may be serious or trivial. In the latter group may be mentioned straining, lifting, or coughing. We recently saw a boy with this condition after jumping across a gate. He missed the gate post but did not strike it with his chest so far as we could tell. Lacerations of the lung or bronchi, chest contusions, concussion blast (see Chapter 14—Shock), excessive positive pressures in mechanical resuscitators, especially in infants, may produce it.

Tension pneumothorax may cause the condition by direct penetration of the mediastinal pleura or by extension along the root of the lung. Conversely, a ruptured lung or bronchus may allow air to enter the mediastinum under the visceral pleura along the lung root without pneumothorax. Soon the air escapes into the subcutaneous tissues of the neck, face, and even the entire body (subcutaneous emphysema).

In the latter instance mediastinal pressure is decreased. Sometimes air enters the pericardium along the pericardial covering of the large vessels, causing pneumopericardium.

The symptoms and signs are typical. There is subcutaneous emphysema of the neck and face, the jugulars stand out, and there is dyspnea and cyanosis. X-ray shows a widened mediastinum and may show air in lateral films. If no subcutaneous emphysema is evident, the picture resembles cardiac tamponade.

Treatment depends upon the cause, but first and foremost is release of air from the mediastinum if possible. A large, No. 18 gauge needle is introduced into the jugulum; usually the relief is dramatic and an audible hissing sound may be heart. Tension pneumothorax must be corrected immediately (see Chapter 19). If the mediastinum fills up again, incision in the jugulum is indicated although mediastinitis is to be feared. If the air cannot be reached by an incision in the jugulum and if pressure symptoms continue, an incision is made over the heart, avoiding the pleura. Even the pericardium may be opened if found necessary.

If the mediastinal emphysema is mild, it should need no active treatment and will be absorbed after the primary cause is corrected. Mild cases without apparent cause need no treatment.

BLOOD VESSELS

Harvey first described the circulation of the blood. He knew that the arteries carried blood from the heart and the veins carried it back, but he could not explain how it got across from arteries to veins. We now know it is by way of the capillaries. These tiny vessels, whose walls are made of a single layer of endothelial cells, carry food and oxygen into the tissue and remove waste products from them. The liver and kidney, interposed in the circulatory system to detoxify and remove waste products from the blood, have two sets of capillaries for blood to pass through before returning to the heart. The lymph vessels are important in carrying paticulate matter away. The arteries (except the pulmonary) carry oxygenated blood, and the veins (except the pulmonary vein) carry oxygen poor blood. (See Chapter 11.)

The large arteries have been termed arteries of storage, while the smaller arterioles, arteries of distribution. These terms are accurate because at any one time about 7 per cent of the blood is in the capillaries and 93 per cent in the large arteries, their main and terminal branches. Some vessels are tortuous, as in the cheeks, tongue, and lips, which are movable, or the uterus, which is expansible. In the liver, spleen, bone marrow, and adenals wide tortuous vessels exist called sinusoids. The distinctive features of the blood vessels in the portal, splenic, renal, and cardiac circulations are discussed under their respective regions. Peculiarities of the pulmonary circulation are reviewed in the chapter dealing with the respiratory system. The flow of blood to all organs can remain suspended for as long as twenty to thirty minutes without any subsequent signs of organic damage provided an adequate supply to the brain is secured. In the experimental animal this has been accomplished by creating an anastomosis between carotid and jugulars on one side to those of another dog of the same size.

Veins have thin walls (which are easily compressible) and valves within the lumen placed usually just distal to the mouth of an entering tributary. They are semilunar, usually in pairs, and their free borders are turned toward the heart. They are composed of endothelium with some fibrous tissue, and the wall of the vein is dilated on the proximal side of each valve into a pouch or sinus. Valves are more numerous in the deep than superficial veins and more numerous in children than in adults. These valves direct the flow toward the heart and are present in all veins except those of the abdomen (the azygos has imperfect valves and valves are present in the testicular veins), the thorax, the brain, and some veins of the face (for example, the angular). Tributaries to the valveless veins in the thorax and abdomen have efficient valves. This arrangement prevents overdistention of the cerebral veins and sinuses in vomiting or coughing and of the veins of the extremities in increased intra-abdominal pressure from ascities or new growth.

Edema of the extremities as a result of increased intra abdominal pressure occurs only if the valves are imperfect. In the experimental animal this mechanism is easily demonstrated. The artery to an extremity is left intact. The vein is divided and its proximal side is ligated. Into the distal segment a cannula is inserted, which is attached by rubber tubing to a manometer. The venous pressure soon equals the arterial pressure. If now the extremity is squeezed, the venous pressure may go much higher than the arterial, due to the valves, which act like a hydrostatic pump. If the pressure in the abdomin increases, so will the pressure in the veins—until systolic pressure is reached; then circulation ceases and the viscera become blanched.

Roughly, the pressure in the vascular tree is highest in the aorta and then decreases until its lowest point is at the right auricle. Venous blood flow depends on the following factors: (1) The contraction of the left ventricle (vis a tergo) supplies the force which keeps the blood stream moving. (2) The subatmospheric pressure within the thorax (−6 mm. of mercury in inspiration to −2.5 mm. of mercury during expiration) expands the veins and literally sucks blood into the thorax. The venous pressure at the

right auricle is +5 mm. of water; therefore, blood enters the thorax easily. (3) The action of the right side of the heart, by quickly emptying the auricle and ventricle, allows blood to flow in unimpeded. (4) The massaging effect of muscles forces blood along the veins. This is most notable in the legs. (5) The effect of gravity in impeding the venous flow is especially important in the veins of the thorax and abdomen (which are valveless) and in varicose veins (in which the valves are functionless).

In vomiting, the diaphragm descends and the abdominal muscles contract. Intra thoracic pressure is increased as is evidenced by the distention of the veins of the neck, although part of this may be due to the head-down position assumed in vomiting. Abdominal pressure is greatly increased and is much more than the intrathoracic pressure. This sends blood up into the thorax. By reflex vagus inhibition the heart stops momentarily and then the next beat is more forceful When the vomiting has ceased, the diaphragm ascends, the abdominal muscles relax, and the blood flows back into the abdomen (no valves). Were it not for such a mechanism there would be an overdistention of the right heart and death from asphyxia. Anoxemia plus stasis causes death of tissue. This is as true of varicose ulcer as of the patient as a whole. In the Trendelenburg position blood flows into the thorax. If there is anoxemia, the heart beat is increased (cardioaccelerators—Bainbridge reflex), but the right ventricle cannot force blood into the inactive lungs, stasis occurs with right-sided cardiac inadequacy, there results a fall in arterial pressure, and death may occur.

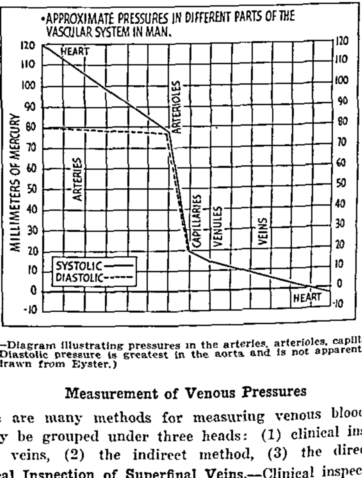

Fig. 175.—Diagram illustrating pressures in the arteries, arterioles, capillaries, venules, and veins. Diastolic pressure is greatest in the aorta and is not apparent in the capillaries. (Redrawn from Eyster.)

Measurement of Venous Pressures

There are many methods for measuring venous blood pressure. These may be grouped under three heads: (1) clinical inspection of superfinal veins, (2) the indirect method, (3) the direct method.

Clinical Inspection of Superfinal Veins.—Clinical inspection is the most widely used method. A few illustrations may be given to illustrate the method.

Jugular Veins.—With the patient in a semisitting position these veins are normally not filled above the plane of the manubrium. Distention of the veins above this level indicates a high venous pressure in the superior vena cava system. If, in addition, there is hepatomegaly with or without leg edema, there may be a general increase in venous pressure as seen in cardiac failure. At times in heart failure the jugulars are not greatly distended unless pressure is put on the abdomen (hepato-jugular reflex).

Veins of the Hand.—With the patient sitting, the arm is slowly raised. The distance of the point at which collapse is observed from the plane of the right atrium (taken as the fourth intercostal space) is a rough measurement of the venous pressure. Normally it is 100 mm. of water. In cardiac tamponade the veins do not collapse even when elevated to 90 degrees.

Veins of the Undersurface of the Tongue.—Veins of undersurface of tongue are inspected while the patient is sitting. These veins are normally collapsed; when distended, the venous pressure is equivalent to 200 mm. of water or more.

Veins of the Leg.—The veins of the leg are observed with the patient in a semireclining position and are useful in tests of peripheral vascular disease and intra-abdominal increase in pressure.

Indirect Method of Determining Venous Pressure.—Indirect method of determining venous pressure as employed by Eyster depends on the principle that the least pressure necessary to cause collapse of a vein is approximately equal to the pressure within its lumen. Various devices have been perfected to determine pressure in this way.

Direct Method of Determining Venous Pressure.—Direct method of determining venous pressure is the usual method employed today. It is done by inserting a needle in the vein (about 19 or 20 gauge). To this needle is attached a three-way stopcock. To one arm a 5 c.c. syringe is attached and to the lateral arm a small rubber tube is fixed to which a glass manometer is attached. The syringe contains physiological saline. First the manometer is filled and then the stopcock is turned and the rest of the saline is injected into the vein. Then the stopcock is turned again, permitting saline to flow into the vein until it reaches its pressure level. The same device without the syringe attachment or three-way stopcock is used in reading splenic vein, portal vein, and pulmonary artery pressures.

Normally the venous pressure varies with the position of the patient, habitus, distance of the manometer from the skin, etc. In the arms it is usually between 50 to 150 mm. of physiological saline solution. The pressure in the femoral vein is a little higher than in the antecubital vein in the same person. In obese people it may be 40 to 50 mm. of saline higher.

TABLE XIV

DIAGNOSTIC VALUE OF REGIONAL DIFFERENCES IN VENOUS PRESSURES
(From Hussey and Jeghers: New England J. Med., 1947.)

PRESSURE DATA	DIAGNOSIS
Diminished in all peripheral veins	Peripheral vascular collapse (shock); syncope
Elevated in all peripheral veins	Right-sided and generalized cardiac failure; constrictive pericarditis (Pick's disease); pericardial effusion; uniform loss of negative chest pressure (obstructive emphysema); Bernheim syndrome; varicose veins
Normal arm and elevated in leg veins*	Ascites; tympanites; pneumoperitoneum; pregnancy; hypernephroma and other tumors of kidney, with invasion of inferior vena cava; primary carcinoma of liver, with invasion of inferior vena cava; primary tumor of inferior vena cava; thrombosis of inferior vena cava; ligation of inferior vena cava; masses in peritoneal cavity; solitary abscess in right lobe of liver; subphrenic abscess on right; echinococcus cyst of liver; large tumor mass in right lobe of liver
Elevated in arm and normal in leg veins	Aneurysm of aorta; ?dilatation of aorta; lymphoma of mediastinum; metastatic masses in mediastinum; primary tumor of mediastinal structures; abscess of mediastinum; thrombosis of superior vena cava
More elevated in one arm than in other and lower or normal in leg veins	Localized obstruction of axillary or subclavian veins due to exertion, pressure from neoplasm, cardiac failure; unilateral chest lesions (pleural effusion, pneumothorax, thoracoplasty); aneurysm of aorta (85 per cent higher on left than on right); aneurysm of innominate artery (higher on right than on left); arteriovenous fistula of arm
More elevated in one leg than in other and lower or normal in arm veins	Arteriovenous fistula of leg; thrombosis of femoral or iliac vein
Dissociation between internal jugular vein and general peripheral venous system	Polycythemia or mass in neck or upper mediastinum (elevated pressure); thrombosis of lateral sinus (diminished pressure)
Elevated in portal vein and normal in arm and leg veins	Cirrhosis of liver; obstruction of portal vein; obstruction of splenic vein; ?Chiari syndrome

*Also observed during abdominal operations.

VASCULAR SURGERY

General Considerations

In Chapter 3 we discussed the mechanisms of repair in various types of tissues and organs, the formation of new capillaries in granulation tissue from endothelial proliferation of the divided capillaries, as well as the restoration of continuity of the endothelium when larger vessels were injured. In Chapter 13 we reviewed the physiology of the circulation, the effects of hemorrhage and plethora, and the reaction of the larger

blood vessels to trauma and methods for the control of such injuries. *In the remainder of this chapter we shall discuss the surgical methods* used in the management of diseases and injuries of the blood vessels and lymphatics. Abnormalities may demand that vessels be ligated, anastomosed, excised, or obliterated.

Ligations

Ligations may be made in continuity. However, ligation and division of an injured vessel is preferable because of the danger of erosion and hemorrhage, or reestablishment of lumen or vasomotor phenomena. The tug on the end of an artery which has been tied in continuity, even though only a fibrous cord remains, may cause pain, poor pulse, or claudication until divided. The local effects of ligation have been described in Chapter 3. However, some facts need to be emphasized. Halsted showed years ago that a silk ligature applied tight enough to obliterate a large artery always cuts the intima and media and this wound *is responsible for the local thrombus.* The diminished pressure and flow within an occluded large artery is also a factor in local thrombus formation. Theoretically, if healing is to occur without thrombosis, intima must be opposed to intima without injury to this layer of endothelium. To achieve this result, bands of fascia (recently cellophane has been employed) are wrapped around the vessels for partial occlusion as often used in carotid incomplete ligation or complete constriction. The partial occlusion reduces the lumen to about 50 per cent and prevents *re-expansion due to fibrosis. If occlusion of the vessel is too great,* the Venturi phenomenon or retrograde flow through collaterals due to the conversion of end pressure of the artery to lateral pressure may cause aneurysmal dilatation peripheral to the narrowing. This same phenomenon is sometimes seen in coarctation of the aorta. The Venturi principle was first described by G. B. Venturi, an Italian physicist (1746-1822), who showed that when there is a reduction in the cross-sectional area of a pipe containing flowing water, there occurs an increase in velocity and a decrease in pressure. The *venturimeter* is an instrument for measuring the flow of liquids such as the blood flow in blood vessels. Since there may be hypertrophy proximal to the stenosis in an artery, the normal vessel distal to the narrowing may dilate due to the sudden increase in lateral pressure as the velocity is quickly slowed. The same caution should be used in doing lateral suture of blood vessels.

For all practical purposes the tying of an artery as usually done produces a thrombus at the site of ligation *which may propagate.* The thrombus forms proximal and distal to the ligature and its propagation is not limited by the nearest sizable branch it may go on.

Effects of Ligations on the Part.—The effect of ligation depends upon the amount of collateral circulation present, degree of vasospasm

engendered, and vulnerability of the tissue. In the final analysis anoxemia of the part is the deciding factor—if the tissues can withstand the decreases in oxygen until collaterals form, they will live. This is the reason for incomplete ligation. The amount of collateral circulation which occurs after tying previously normal major vessels is fairly well known, due to military and civilian experience in injuries which demand ligation, as is also the degree of vasospasm and vulnerability of tissue. A ligature acts as a severe trauma and produces vasoconstriction distally. If, however, the artery is divided between ligatures, or if the sympathetics are interrupted by injection of local anesthetic into the ganglion, or if ganglionectomy is done, vasoconstriction does not occur. Obviously simply dividing the injured vessels between ties is the method of choice; other methods mentioned are used if this fails. However, vasoconstriction should be dealt with promptly. Since cold, pain, fear, anger, asphyxia, hemorrhage, or dehydration are common causes for vasoconstriction, measures are instituted to avoid such factors. Whether ischemia progresses to recovery or not depends upon the volume of blood the limb receives, the pressure at which it is delivered, the length of time the ischemic state has existed, and the metabolic demands of the limb itself. Since re-establishment of circulation depends on collaterals, every ligation should be done with a minimum of trauma and under aseptic conditions. Extensive débridement may cause thrombosis in the collaterals, or a large hematoma may compress them, in either case causing gangrene. Shock due to its lowering of blood pressure may so decrease peripheral circulation as to cause ischemia. For this reason blood transfusion is imperative. Holman believes that a large artery should be tied just beyond a large collateral vessel or branch so that the full force of arterial pressure is used to expand this collateral and its branches. The ligature which is applied distal to the injury is placed just proximal to a large branch if feasible. In general the following disturbances may result from the ligation of large arteries: (1) destruction of tissue varying from local necrosis in muscles (ischemic myositis or Volkmann's ischemic contracture) to gangrene; (2) functional disorders due to reduced blood supply such as intermittent claudication; (3) vasomotor phenomena, trophic disorders, cyanosis, sweating, cold extremities, etc.

The danger of occlusion to the common or internal carotid is that of cerebral damage due to anoxemia which results in hemiplegia and aphasia. This danger is less in the young than in the aged. The innominate and subclavian may be tied without serious effects if exposure is good. The occluded axillary artery may cause gangrene in the lower forearm and hand in the older individual but is less apt to do so in the younger. The ligated brachial is less apt to cause trouble if tied distal to the profunda or the superior ulnar collateral. Ligation of the common, external, or internal iliacs usually do not cause gangrene. The super-

ficial or deep femorals compensate for each other. A tie on the popliteal is followed by gangrene in 70 per cent, ischemic myositis in about 25 per cent—6 per cent escape permanent effects.

Secondary hemorrhage with repeated ligations implies much thrombosis to collaterals and gangrene with possible infection and death. Ligation beneath mucous membranes or near the mouth, nose, anus, or vagina are apt to be infected unless precautions are taken. A good sign at the time of ligation is bleeding from the distal segment of the artery. Tying of the concomitant vein does not improve the chance for recovery but does not hinder it and is therefore commonly done in the hope that collaterals may form more quickly. Even though the distal pulses are absent, a limb will probably survive if active movement of the digits is present and if they are warm, have sensation, and good color. The pulse will return only when the collaterals are wide and short; if narrow and long, *the pulse is not felt because it is lost in its transit back to the main artery.*

Exposure of Blood Vessels.—In accidental wounds, ligations are usually done at the site of the injury. However, the injured vessel may be badly torn and, if large, may not be properly controlled by ligature because of an exsanguinating hemorrhage, or the vessel may be cut and an anastomosis may be indicated; in either event, a temporary or permanent ligature is advisable proximal to the tear. Aneurysm or arteriovenous fistula also demand proximal control—in fact, such control is as essential to successful vascular surgery as the control of spillage in the bowel surgery and certainly more apt to be lethal. Most textbooks on applied anatomy describe the anatomical considerations, involved in ligations. Here we can only outline a few general rules. (1) Although ligations are lifesaving, yet some consideration should be given to the cosmetic result of incisions made for this purpose. Skin creases are followed, not cut vertically, for reasons given in Chapter 3. In the neck a transverse incision heals with a minimum of scarring but such incisions are not always feasible. In the cubital and popliteal spaces the same rule is followed; if insufficient exposure is obtained, then the incision is enlarged by converting the transverse opening into a ⌐—˩ or S- or Z-shaped incision. (2) The base of the neck contains the innominate, subclavians, and carotids. To reach them the clavicle should be removed subperiosteally, wholly or partly, as indicated. If the sternal end is removed, the cartilage should be excised and then a vertical incision *through the periosteum* exposes the innominate and carotid. A wider exposure of the vessels in the superior anterior mediastinum is secured by the Sauerbruch operation or its modifications. The sternum is split down to the level of the third interspace, with Schumacher sternal shears, or the Lebsche sternum splitter or the Bethune bone-cutting forceps, and across into the right and left third interspace and the sternum spread apart. In addition, the inner third of the right or left clavicle or both

may be resected. Through the central portion of the clavicular bed the subclavian vessels and brachial plexus are reached. Division of the scalenus anticus exposes the vertebral at its origin and the thyrocervical trunk. Prolongation of the incision laterally in the groove between the pectoralis major and deltoid leads to the cephalic vein—a guide to the axillary vessels as every surgeon knows who has performed radical mastectomy. (3) The vertebral vessels, according to Elkin, are best described in three parts: (a) the part passing from its origin in the subclavian artery to the foramen in the transverse process of the sixth cervical vertebra is best reached through an incision parallel to the fibers of the sternomastoid muscle and over the interval between its sternal and clavicular heads; (b) the part which runs through the foramina of the transverse processes of the upper six cervical vertebra is exposed through an incision along the anterior border of the sternomastoid muscle which is retracted laterally; the carotid sheath is held aside medially and the scalenus anticus is retracted laterally or divided from its origin on the transverse processes which are exposed and one or more rongeured away; (c) the third part extends from the foramen in the atlas to the occipital foramen. It is exposed through an incision high and parallel with the sternomastoid muscle which is detached from its insertion and turned downward posteriorly. The tip of the transverse process of the atlas is identified and the origin of the levator scapulae muscle is cut and turned down. (4) To approach vessels within the thoracic cage, portions of the first and second ribs with a variable segment of the sternum are removed. (5) The brachial vessels are easily exposed on the medial side of the arm through a cut along the biceps edge and the ulnar and radial through longitudinal incisions on their respective sides of the forearm. (6) The iliac vessels are approached through an incision above and parallel with the inguinal ligament. The peritoneum and abdominal contents are retracted medially. (7) The femoral vessels lie medial to the sartorius muscle in their proximal portion and behind this muscle in their distal parts. An incision medial to this muscle high in the thigh or anterior to it lower down will give good exposure after the muscle is retracted. (8) The anterior and posterior tibial and peroneal vessels are best exposed at their origin by removing subperiosteally the upper portion of the fibula through an incision over it, being careful not to injure the common peroneal nerve. (9) The incision for exposure of the tibial and peroneal vessels lower in their course is made on the medial side of the leg posterior to the tibia. (10) The plantar vessels are approached on the medial side of the foot rather than through the sole, thereby avoiding a scar on the weight-bearing area.

Type of Ligature.—Much has been written concerning ligature material and the respective merits of the material fully reviewed. We have already described the use of fascia for incomplete ligation of large vessels, although metal bands, rubber bands, and cellophane have also been

used for this purpose. In general, it is our custom to use catgut in infected or potentially infected areas—the size of the gut varies with the size of the vessel. We have not found it necessary to use a size larger than No. 1 chromic. Ligations of large vessels are usually best accomplished by using a large size silk (No. 1 or 2) or cotton. We have preferred these sutures because they are more pliable and easier to handle when the vessels are transfixed. For the largest arteries some surgeons use small umbilical tape. We have used this material as a temporary or holding ligature and also as a tie. A single knot is made and the edges sutured with silk or cotton. Then a transfixion ligature is placed distal to this. We are now using large-sized waxed silk and find this entirely satisfactory. The method of ligating is perhaps as important as the material employed. In Chapter 3 diagrams of methods used are depicted; in Chapter 21 the illustration of handling the subclavian vessels in complete disarticulation of the shoulder is depicted. All large vessels are first tied proximally and distally, leaving enough space to put in at least a proximal transfixed ligature. If space allows, two transfixed ties are put in and the vessel divided between them. Transfixion may be accomplished by a single or double suture through the vessel as shown in Chapter 3 or by a purse-string type of ligature as is sometimes used in obliterating a patent ductus arteriosus. In pneumonectomy the pulmonary vessels are dissected out and the branches are tied distally. This leaves a flare distal to the proximal ligatures. Other materials used for ligation are hemp, ox aorta, ox peritoneum, kangaroo tendon, silver wire, etc.

Complications of Ligations.—These have already been mentioned. They may be summarized here as follows: (1) Secondary hemorrhage due to cutting through of ligature, necrosis, or infection. (2) Thrombosis with propagating thrombi leading to embolism or occlusion of collaterals due to various factors such as trauma at the time of injury, extensive débridement, infection, exposure to cold, loss of large volume of blood with resulting hypotension. The organization of a thrombus is facilitated chiefly through the media. The organized thrombus occurs in a regular and concentric form in the young and in an irregular manner in the old. The vessels that invade the thrombus run parallel to it if it is aseptic; if infected the penetrating vessels diverge radially. The inflammatory reaction about a thrombus extends beyond the adventitia of the artery to the walls of adjacent veins and nerves but does not involve the concomitant vein as often as venous thrombosis involves the neighboring artery. (3) Aneurysmal dilatations. (4) Effect on the extremity as previously described.

Anastomosis

The restoration of vascular continuity is desirable wherever and whenever possible. Moreover, if ligation of the vessel is known to carry a great chance for gangrene, anastomosis may be done in the hope that

the extremity will remain viable long enough for collaterals to form, even though ligation will be necessary later. At the outset we must remember that ligation is a lifesaving measure and if a patient has multiple injuries, as is usually the case, or if his condition is poor, anastomosis had better not be tried. There are other contraindications: extensive trauma to a limb which is badly crushed, making restoration of circulation unlikely and resulting in gangrene due to devitalization by the crushing force; a long period of avascularity (experiments tend to show that if an extremity is not warmed, skin will survive at least twenty-four hours; muscle, six to ten hours; nerve tissue less); and lastly, poor hospital facilities. Anastomosis will be found most satisfactory then in incised wounds or bullet wounds seen early with good hospital facilities. However, as a temporary measure, no matter what the condition of the wound itself, anastomosis may be attempted.

Methods of Anastomosis.—Smaller vessels are less apt to stay open than larger ones, but this is not deterrent. The adventitia has no tensile strength; bits of it may be carried into the vessel lumen and therefore it is pushed back and not included in the suture. After suturing is complete, it is worked back over the stitch line, carrying its vaso vasorum with it and thereby nourishing the media. Thus stitches go through intima and media. Sutures should be of fine waxed silk No. 00000 placed close together and may be continuous or interrupted, over-and-over, or mattress. Ideally, the mattress eversion stitch bringing intima to intima with no thread exposed intralumenally is best. Practically any method of suturing is good provided loose ends do not wave in the blood stream, producing thrombosis and the propagation of the clot. Constriction of the lumen may cause a turbulence and a clot peripheral to the constriction which propagates. Torsion of the vessel will have a similar effect.

If ideal conditions do not prevail for direct suture or if the gap is wide, nonsuture methods or suture with mechanical aids should be tried. Various devices have been tried: venous grafts with and without Vitallium tubes; plastic, silver, glass tubes; absorbable cellulose; molded fibrin and gelatin tubes. If a vein graft is used, the distal end of the vein is anastomosed to the proximal end of the artery. Recently Blakemore and colleagues have combined the use of Vitallium tubes and venous grafts with good results in traumatic injuries, restoration of arterial continuity after excision of arteriovenous fistula and after excision of arterial aneurysm, portal-caval anastomosis in portal or splenic hypertension (Laennec's or portal cirrhosis; congestive splenomegaly or Banti's syndrome) and splenic-renal vein anastomosis following splenectomy in Banti's syndrome. The use of anticoagulants such as Dicumarol and heparin has been advocated in venous anastomoses and venous grafts and all tube types of restoration of continuity, whereas their use in arterial suture has not seemed warranted. Heparin subcutaneously as out-

lined in Chapters 6 and 13, keeping the clotting time at about 20 minutes, would seem to be indicated in all graft types of restoration of continuity; however, the danger of hemorrhage probably outweighs the danger of thrombosis and therefore anticoagulants are not universally employed.

CONTUSIONS AND WOUNDS OF ARTERIES

Contusions

Contusions of arteries may be followed by an inflammatory change or *arteritis*. This leads to *thrombosis* and ultimate obliteration of the vessel or embolism. Resection of the contused portion of such an artery may release spasm and aid the cold, blue, painful extremity to become normal again. If seen early, ten to twelve hours, the thrombus may be removed. Spasm of an artery is seen as a temporary effect after contusions, wounds, and fractures. Pulsation is temporarily absent and the extremity becomes cyanotic and cold. This spasm is a compensatory mechanism to reduce hemorrhage and prevent clotting in the vessels which will be required for collaterals. It is unwise to interfere with this process early because collaterals will have their best chance to function when end pressure is increased, forcing more blood into collaterals. Later, should vasoconstriction persist, sympathectomy may be indicated.

Other important considerations of arterial contusion are the secondary effects such as weakening of the arterial wall with subsequent rupture and hemorrhage; pulsating hematoma may follow late rupture and hemorrhage into surrounding tissues with formation of a sacculated false aneurysm. *Concussion* of an artery may produce temporary spasm. In all wounds where contusion or concussion has occurred, careful exploration is indicated. The former requires excision of the contused portion, the latter perhaps a periarterial sympathectomy which is really done to inspect the vessel wall. The introduction of drains in a wound with sutured or ligated large blood vessels is dangerous and should not be done; in fact, no foreign bodies, including the sulfonamides, should be introduced.

Wounds

Wounds of arteries may be complete or incomplete. A complete wound is one which traverses the entire vessel wall. It may be a clean incised wound which may be longitudinal or tangential or transverse. We have noted in previous chapters (Chapters 3 and 13) that the former bleed more freely than the latter, which retract. The wound may be a lacerated one in which a part of the vessel has been torn away. Lastly, the concomitant vein may have been injured. Complete wounds are treated by one of the following methods:

1. Ligation is a lifesaving measure. We have already discussed this procedure previously; however, some facts need emphasis. Ligation and

the extremity will remain viable long enough for collaterals to form, even though ligation will be necessary later. At the outset we must remember that ligation is a lifesaving measure and if a patient has multiple injuries, as is usually the case, or if his condition is poor, anastomosis had better not be tried. There are other contraindications: extensive trauma to a limb which is badly crushed, making restoration of circulation unlikely and resulting in gangrene due to devitalization by the crushing force; a long period of avascularity (experiments tend to show that if an extremity is not warmed, skin will survive at least twenty-four hours; muscle, six to ten hours; nerve tissue less); and lastly, poor hospital facilities. Anastomosis will be found most satisfactory then in incised wounds or bullet wounds seen early with good hospital facilities. However, as a temporary measure, no matter what the condition of the wound itself, anastomosis may be attempted.

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matory changes to develop around the extravasated blood with the formation of a fibrous wall or sac. This is known as a *false aneurysm* since the wall of the sac is made of fibrous tissue. If the adventitia and media have been injured, allowing the intima to bulge, a true aneurysm is formed which contains portions of intima and media. Aneurysm may also result from nontraumatic injury, chief of which is *bacterial invasion.* This is particularly true of the ascending aorta and aortic arch. In general, an aneurysm of the aorta or the largest vessels in the body is usually bacterial; smaller and more peripheral arteries develop aneurysms more commonly from traumatic injury. The *Spirocheta pallida* is the most common offender, causing a syphilitic arteritis late in the disease. The organisms reach the vessel wall through the vasa vasorum, which in turn become obstructed due to intimal proliferation. As a result of this obstruction, the nutrition of the tunica media is impaired, resulting in a degeneration of the muscle fibers and replacement by fibrous tissue which stretches under the lateral pressure exerted by pulsations, causing a fusiform or saccular dilatation. Another type of bacterial damage is seen in mycotic aneurysms. Here an infectious arteritis results from: (1) Local suppurative process (pulsating abscess as seen in suppurating lymph nodes, retropharyngeal, peritonsillar abscess, or abscess anywhere adjacent to a large artery). (2) Tuberculosis or actinomycosis with involvement of the media and aneurysm or even rupture of the artery. (3) Emboli may lodge in the vasa vasorum with the formation of a local abscess in the arterial wall—this mycotic embolic arteritis is seen in subacute bacterial endocarditis, typhoid fever, pneumonia, or other septicemias. Usually mycotic aneurysms are found in peripheral, unprotected arteries (popliteal, femoral, axillary, brachial) but may be seen anywhere. We have seen them in the superior mesenteric and renal arteries in cases of subacute bacterial endocarditis, the former in a girl 10 years of age. It should be added that an aneurysm may itself be the seat of subacute bacterial endarteritis giving rise to emboli. (4) Periarteritis nodosa and other types of necrotizing arteritis in which the medial coat shows localized areas of necrosis may cause aneurysms in small and medium-sized arteries. The causative organisms are not known. Other causes of aneurysm are: (1) Arteriosclerosis. This is the most common cause of aneurysm of the extremities in those over 50 years of age. The localized destruction of the medial coat is probably the result of impaired nutrition from thickening and compression of the vasa vasorum. The arteries have deposits of calcium and are friable which accounts for the fact that arteriosclerotic aneurysms are seen where the vessel is peripheral, unprotected by muscle, and subject to the strain of bending as in the popliteal and femoral regions. We have recently seen bilateral arteriosclerotic aneurysms of the femoral arteries in a man 58 years old with arteriosclerosis. (2) Congenital defects where there is a localized weakness of the media. The intracranial vessels—internal carotid, anterior

division is preferable to ligation in continuity due to the possibility of erosion of the vessel or re-establishment of the lumen through partial necrosis of tissues within the ligature. Also, the danger of vasomotor phenomena and pain as a late complication should be remembered. Ligation of the concomitant vein is strongly urged by some and condemned by others. Those who advocate it aver that the incidence of gangrene is decreased by 12 to 15 per cent. There is a great difference of opinion in various studies of battle casualties. Those who use it claim that reducing the rate of venous return permits better peripheral nourishment by inducing colaterals to form due to an increase in venous, capillary, and arteriolar pressures, respectively. In civilian practice it is wise to ligate the large vein which accompanies the torn artery because it is usually contused, if not torn, and is a fruitful source of thrombosis and possible embolism. If the distal segment pulsates (Henle-Coenen phenomenon), this is evidence of good collateral circulation and the vein need not be ligated. The extremity should not be warmed.

2. Suture repair has also been discussed. Clean wounds involving less than half the circumference give the best results, although any wound seen early may be repaired, using fine silk through all the coats (some authors advise not including the intima; others do not include the adventitia). Heparin should be used for twenty-four hours at least. The size of the vessel may be reduced by one-half and still have 75 per cent of normal blood flow through it.

3. Nonsuture anastomosis with Vitallium, plastic, or glass tubes or vein segments may be tried if facilities are available. Even though unsuccessful, this measure may provide for blood flow long enough to allow collaterals to form, even though later ligation and resection may be necessary. Bleeding from the distal segment is a good sign.

4. Nonsurgical therapy may be used in small wounds of vessels in which hemorrhage may be controlled by pressure. Even though a false aneurysm may form, this can be excised after collaterals form. In addition to the surgical measures outlined, supplemental therapy includes anticoagulants, sympathetic block or sympathetic ganglionectomy, fasciotomy to relieve external pressure, oxygen, and posture (heart level or higher).

Incomplete wounds are more apt to form pulsating hematomas which in time form a false aneurysm. Also, as a result of small incomplete wounds in arteries, true aneurysms occur. If the neighboring vein is also injured, arteriovenous fistula results. Cirsoid aneurysm or aneurysmal varix, while usually congenital, may result from large arteriovenous fistula. In pre-existing vascular nevi, injury may accentuate the lesion and convert a small hemangioma into a plexiform or racemose angioma.

Aneurysms.—Injury to an artery may permit the outpouring of blood into surrounding tissue, forming a hematoma which pulsates. The hematoma temporarily stems the flow of blood, allowing time for inflam-

matory changes to develop around the extravasated blood with the formation of a fibrous wall or sac. This is known as a *false aneurysm* since the wall of the sac is made of fibrous tissue. If the adventitia and media have been injured, allowing the intima to bulge, a true aneurysm is formed which contains portions of intima and media. Aneurysm may also result from nontraumatic injury, chief of which is *bacterial invasion.* This is particularly true of the ascending aorta and aortic arch. In general, *an aneurysm of the aorta or the largest vessels in the body is usually* bacterial; smaller and more peripheral arteries develop aneurysms more commonly from traumatic injury. The *Spirocheta pallida* is the most common offender, causing a syphilitic arteritis late in the disease. The organisms reach the vessel wall through the vasa vasorum, which in turn become obstructed due to intimal proliferation. As a result of this obstruction, the nutrition of the tunica media is impaired, resulting in a degeneration of the muscle fibers and replacement by fibrous tissue which stretches under the lateral pressure exerted by pulsations, causing a fusiform or saccular dilatation. Another type of bacterial damage is seen in mycotic aneurysms. Here an infectious arteritis results from: (1) Local suppurative process (pulsating abscess as seen in suppurating lymph nodes, retropharyngeal, peritonsillar abscess, or abscess anywhere adjacent to a large artery). (2) Tuberculosis or actinomycosis with involvement of the media and aneurysm or even rupture of the artery. (3) Emboli may lodge in the vasa vasorum with the formation of a local al scess in the arterial wall—this mycotic embolic arteritis is seen in subacute bacterial endocarditis, typhoid fever, pneumonia, or other septicemias. Usually mycotic aneurysms are found in peripheral, unprotected arteries (popliteal, femoral, axillary, brachial) but may be seen anywhere. We have seen them in the superior mesenteric and renal arteries in cases of subacute bacterial endocarditis, the former in a girl 10 years of age. It should be added that an aneurysm may itself be the seat of subacute bacterial endarteritis giving rise to emboli. (4) Periarteritis nodosa and other types of necrotizing arteritis in which the medial coat shows localized areas of necrosis may cause aneurysms in small and medium-sized arteries. The causative organisms are not known. Other causes of aneurysm are: (1) Arteriosclerosis. This is the most common cause of aneurysm of the extremities in those over 50 years of age. The localized destruction of the medial coat is probably the result of impaired nutrition from thickening and compression of the vasa vasorum. The arteries have deposits of calcium and are friable which accounts for the fact that arteriosclerotic aneurysms are seen where the vessel is peripheral, unprotected by muscle, and subject to the strain of bending as in the popliteal and femoral regions. We have recently seen bilateral arteriosclerotic aneurysms of the femoral arteries in a man 58 years old with arteriosclerosis. (2) Congenital defects where there is a localized weakness of the media. The intracranial vessels—internal carotid, anterior

division is preferable to ligation in continuity due to the possibility of erosion of the vessel or re-establishment of the lumen through partial necrosis of tissues within the ligature. Also, the danger of vasomotor phenomena and pain as a late complication should be remembered. Ligation of the concomitant vein is strongly urged by some and condemned by others. Those who advocate it aver that the incidence of gangrene is decreased by 12 to 15 per cent. There is a great difference of opinion in various studies of battle casualties. Those who use it claim that reducing the rate of venous return permits better peripheral nourishment by inducing colaterals to form due to an increase in venous, capillary, and arteriolar pressures, respectively. In civilian practice it is wise to ligate the large vein which accompanies the torn artery because it is usually contused, if not torn, and is a fruitful source of thrombosis and possible embolism. If the distal segment pulsates (Henle-Coenen phenomenon), this is evidence of good collateral circulation and the vein need not be ligated. The extremity should not be warmed.

2. Suture repair has also been discussed. Clean wounds involving less than half the circumference give the best results, although any wound seen early may be repaired, using fine silk through all the coats (some authors advise not including the intima; others do not include the adventitia). Heparin should be used for twenty-four hours at least. The size of the vessel may be reduced by one-half and still have 75 per cent of normal blood flow through it.

3. Nonsuture anastomosis with Vitallium, plastic, or glass tubes or vein segments may be tried if facilities are available. Even though unsuccessful, this measure may provide for blood flow long enough to allow collaterals to form, even though later ligation and resection may be necessary. Bleeding from the distal segment is a good sign.

4. Nonsurgical therapy may be used in small wounds of vessels in which hemorrhage may be controlled by pressure. Even though a false aneurysm may form, this can be excised after collaterals form. In addition to the surgical measures outlined, supplemental therapy includes anticoagulants, sympathetic block or sympathetic ganglionectomy, fasciotomy to relieve external pressure, oxygen, and posture (heart level or higher).

Incomplete wounds are more apt to form pulsating hematomas which in time form a false aneurysm. Also, as a result of small incomplete wounds in arteries, true aneurysms occur. If the neighboring vein is also injured, arteriovenous fistula results. Cirsoid aneurysm or aneurysmal varix, while usually congenital, may result from large arteriovenous fistula. In pre-existing vascular nevi, injury may accentuate the lesion and convert a small hemangioma into a plexiform or racemose angioma.

Aneurysms.—Injury to an artery may permit the outpouring of blood into surrounding tissue, forming a hematoma which pulsates. The hematoma temporarily stems the flow of blood, allowing time for inflam-

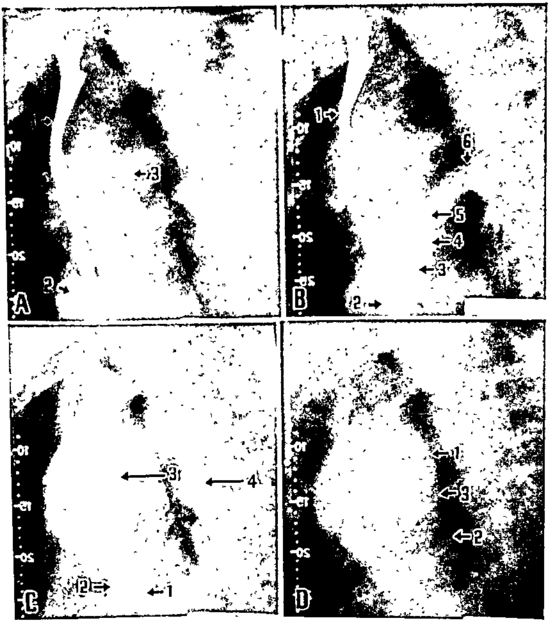

Fig 176*b*.—Angiocardiogram showing aortic aneurysm. *A*. Left anterior oblique angiocardiogram at ⅓ second interval showing opacification of superior vena cava (*1*) and right atrium (*2*) Note large density inseparable from vasculature at base of heart (*3*). *B* Left anterior oblique angiocardiogram at 1½ second interval. Superior vena cava (*1*), right atrium (*2*), right ventricle (*3*), inferiorly displaced main pulmonary artery (*4*), right branch of pulmonary artery (*5*), and left branch of pulmonary artery (*6*). *C*. Left anterior oblique angiocardiogram at 10-second interval showing opacification of left ventricle (*1*), aortic conus (*2*), aneurysm of ascending aorta (*3*), descending aorta (*4*) *D*. Left anterior oblique angiocardiogram at 11½ second interval showing more complete filling of aneurysmal sac with opaque dye. Note marked encroachment on aortic window (*1*) with inferior displacement of pulmonary arteries (*2*), and posterior displacement of trachea (*3*). Dicetyl phosphate, 0.9 per cent, in olive oil was used around the aneurysm with resulting fibrosis and great improvement in all of the patient's symptoms (persistent cough, hoarseness, shortness of breath, and pain).

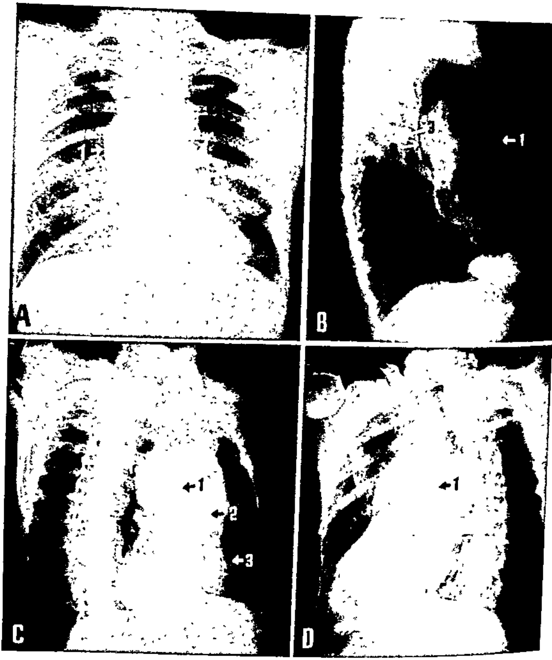

Fig. 176a.—Aneurysm of the ascending arch of the aorta, saccular type. X-ray photographs showing aortic aneurysm. *A.* Posteroanterior teleroentgenogram showing mediastinal mass blending with shadow of ascending aorta (*1*). *B.* Lateral chest film showing large smoothly contoured density in retrosternal area inseparable from ascending aorta (*1*) and compressing trachea posteriorly at (*2*) Note slight vertebral erosion (*3*). *C.* Left anterior oblique film showing loss of aortic window (*1*) double density of mass on ascending aorta (*2*), and projecting anterior border of right ventricle at (*3*). *D.* Right anterior oblique film showing double density of mediastinal mass (ascending aorta) (*1*). This mass is inseparable from aortic shadow in all projections, a finding consistent with aortic aneurysm (see Fig. 176*b*, *A*, *B*, *C*, and *D*).

The teleroentgenograms reveal the presence of a mass which presumably is an aneurysm but which cannot be definitely proved so. Fluoroscopic examination did show pulsations, and this was interpreted as pulsations of the aneurysm. However, this could be transmitted and, therefore, was not positive. Angiocardiograms in Fig. 176*b* definitely prove this opacity to be an aneurysm of the ascending arch of the aorta, saccular in type.

proximal to an aneurysm has no effect on pulse rate or blood pressure, whereas pressure proximal to an arteriovenous fistula or over the fistula causes a slowing of the pulse and an increase in blood pressure. The continuous thrill and bruit and venous engorgement with edema all serve to identify the fistula. Diagnosis of aneurysms is greatly facilitated by angiography and aortography.

Treatment.—Treatment must be directed at removal of the aneurysm or its obliteration by plication and occlusion of new vessels which enter it. In a few cases the continuity of the vessel may be restored. As a rule, the success of the operation in the extremities depends on adequate collateral circulation. Aneurysms of the large arteries of the chest and abdomen require anastomosis as a rule. Rarely sufficient collateral blood supply will form to permit even aortic resection (see coarctation). If the aneurysm involves an artery to a dispensable organ, the organ may have to be sacrificed; namely, kidney, spleen, lung. In vascular injuries, especially if good surgical facilities are not available, it may be wise to allow an aneurysm to form, permitting collaterals to develop, whereas immediate ligation of the wounded vessel may result in gangrene. Obviously this policy cannot be adopted in the face of a rapidly increasing hematoma which threatens the circulation.

The time for operation depends upon adequate collateral circulation even though resection and anastomosis is contemplated. This is true in the latter instance because thrombosis may occur at the site of anastomosis. The development of collateral circulation will usually be advanced enough three months after injury to permit aneurysmal extirpation. However, in nontraumatic and traumatic types various methods are employed to facilitate the development of collaterals. These methods may be listed under the following headings: (1) Chemical. Drugs, such as whiskey, acetylcholine, papaverine, tetraethylammonium chloride or bromide, Priscoline hydrochloride, and cessation of smoking may be tried. (2) Nervous. Interruption of sympathetic action by injection of 1 per cent Novocain daily into the ganglia or preferably by their surgical extirpation or repeated caudal blocks may be used. (3) Mechanical. Measures such as intermittent occlusion of the artery, by hand compression or with the aid of mechanical devices, is often useful, as is also incomplete ligation with fascial band used chiefly in the cerebral aneurysms which demand occlusion of the common carotid artery. This last method is used whenever a large artery is tied for the removal of an aneurysm; that is, the ligature is not pulled snug at one time—three to five minutes are allowed to complete the procedure. This brief interval permits some readjustment on the arterial and particularly the venous side which, due to arterial vasoconstriction, allows venous stasis to occur, thereby suddenly trapping a large quantity of blood in the extremity.

Tests for collateral circulation before surgery are many and varied. Matas suggested compression of the artery proximal to the aneurysm.

portion of circle of Willis—are the most common sites. Rarely they rupture, causing intracranial hemorrhage in the young. Other vessels are rarely involved.

Aneurysms, traumatic or otherwise, therefore may involve any artery in the body. In addition to false and true varieties as previously defined, the pathological types are known as (1) fusiform, which cause a general or uniform dilation of a segment of the artery, (2) saccular, in which there is an outpouching of the vessel wall, and (3) dissecting, which causes a cavity between the layers of the arterial wall due to rupture and which dissects its way between the layers, rupturing to the outside or back into the lumen of the vessel at a distant point.

The symptoms and signs will vary with the type and location of the aneurysm. In the brain, small aneurysmal dilations give no symptoms or demonstrable signs, whereas large ones resemble a brain tumor. In the thorax they may mimic a mediastinal tumor, which indeed they are. Pain from erosion of vertebrae, ribs, or sternum, cough and dyspnea from pressure on the trachea and bronchi, hoarseness, and "goose" cough from recurrent laryngeal nerve pressure are symptoms of progressive pressure of the aneurysm. Signs of aortic regurgitation may occur when the ascending aorta is involved but without cardiac hypertrophy as in arteriovenous fistula. Innominate, carotid, and subclavian aneurysms may be seen and felt usually and cause sensory and motor changes in the arm due to pressure on the brachial plexus and Horner's syndrome from pressure on the cervical sympathetics. Vertigo and syncope result from carotid aneurysms. In the abdomen the chief symptom is pain. In thin people a pulsating mass may be felt.

Aneurysm of an extremity presents an expansile mass which may disappear when pressure is made on its proximal side. The blood pressure distal to the aneurysm is lower than in similar locations elsewhere. Sometimes there is interference with venous and lymphatic return resulting in edema and muscle anoxemia on exercise; therefore, intermittent claudication may result. Rarely there is redness, heat, and tenderness over a true and especially a false aneurysm so that a local inflammation is suspected. The expansile pulsation and interrupted systolic or diastolic or biphasic bruit on auscultation will usually give the clue. However, this is often attributed to transmitted pulsation and compression of the underlying vessel. Not infrequently both conditions are present—that is, an abscess which eroded or weakened the vessel wall to such a degree that an aneurysm has resulted; on incision, after pus has been evacuated, there may be a sudden devastating hemorrhage; therefore simple aspiration is done first.

Pulsating vascular tumors may resemble an aneurysm and arteriovenous fistula is often mistaken for one.

Before any treatment is instituted, an arteriovenous fistula should be ruled out because ligation proximal may embarrass the circulation further or interfere with the circulation of the extremity. Pressure made

Fig. 177.—Diagrams illustrating methods of treating aneurysms. *A*. Older methods. (*1*) Method of Antyllus, third century A. D. The aneurysm was ligated proximally and distally and the sac was opened and packed with lint. This method produced some cures. (*2*) Method of Annell. This operation was first performed about 1710. The ligation is on the proximal side of the sac. As can be seen, collaterals form very quickly and the aneurysm is not cured. (*3*) The method of John Hunter. This was first reported about 1786. The ligation is proximal at a distance from the sac. It can be easily seen that such a method would lend itself to reformation due to collaterals. (*4*) Method of Brasdor. This was reported about 1760. It consists of ligation distal to the sac before any branches are given off. This frequently failed to produce a cure. (*5*) Wardrops modification of the Brasdor operation consisted of tying one of the branches of the artery beyond the aneurysm. This method also failed to produce a cure.

B. Method of treatment of aneurysm from within. The operation is known as endoaneurysmorrhaphy. It was first described by Matas in 1889 and consists of opening the sac and tying off all the collaterals from within and then obliterating the sac. There are three varieties of this operation which Matas reported at that time. One is called the obliterative endoaneurysmorrhaphy without arterioplasty. This is the operation in which no regard is had for restoration of the continuity of the blood vessel, the collaterals taking care of the circulation to the extremities. (*1*) The openings of entrance and exit of the vessel and all collateral openings are closed. (*2*) The second row of sutures begins the obliteration of the fusiform sac. (*3*) Final sutures which completely obliterate the sac. The second is known as endoaneurysmorrhaphy with partial arterioplasty. This is indicated in the saccular types of aneurysms in which there is one opening between the vessel and the sac. (*1*) The opening is closed and the vessel is allowed to remain patent. (*2*) The sac is then imbricated or extirpated, as the case may be.

C. The third variety is endoaneurysmorrhaphy with complete arterioplasty. This operation seeks to restore arterial continuity, a new channel being made out of the sac walls by simply folding these walls over a rubber guide or tube and suturing them firmly together so that the continuity of the artery is maintained. The catheter is withdrawn, of course, before the final sutures are placed. A diagram of what might be considered the modern concept of this operation is shown in (*1*), where a vein graft is placed within the lumen of the sac, and this is sutured to the opening of entrance and the opening of exit and (*2*) complete excision of the sac with vein graft in place.

D. Arteriovenous fistula with aneurysm. This may be treated by transvenous obliteration of the opening and then imbrication or extirpation of the aneurysmal sac. (*1*) The vein is ligated above and below the fistula. (*2*) The opening is closed without the occlusion of the artery. (*3*) The sac is obliterated. This method is also useful in the treatment of false aneurysms. Here the artery is temporarily occluded, the sac is opened, the opening in the artery closed, and the sac is obliterated. This method is known as transsaccular obliteration.

E. Methods of treating aneurysms of the aorta. (*1*) Wiring. The introduction of wire was first used by Moore of London in 1864. The details were improved by Corradi in 1879. The earlier attempts were to use wire through a small hypodermic needle (the wire was either gold or silver) and then electric current was employed using about 40 to 80 milliamperes. Today electrolysis is not often used. Wiring is useful in the saccular types of aneurysm. (*2*) Wrapping the aneurysmal sac with cellophane or Polythene film. Here the mediastinal pleura is lifted up and the sac is wrapped partially or completely if possible with Polythene film. The mediastinal pleura is closed over the wrapping (*3*) Periaortic injection with dicetyl phosphate. This method consists of injecting 9/10 of 1 per cent dicetyl phosphate in olive oil. Since the dicetyl phosphate is probably the active ingredient in the Polythene film which produces fibroplasia, this method seeks to produce the same effect without the danger of uncovering the aneurysmal sac.

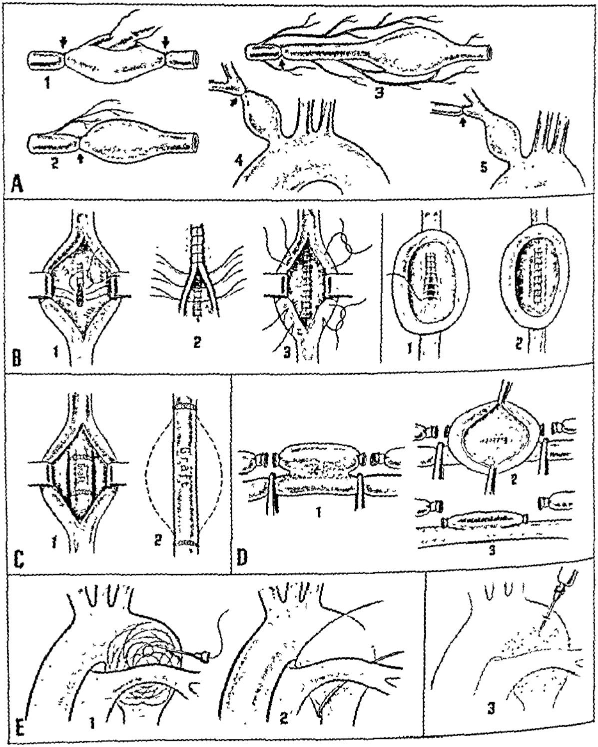

Fig. 177.—*See opposite page for legend.*

dissection can be safely done, inside suture and tamponade may be used or the latter alone where the patient's condition demands immediate cessation of the operation.

Carotid aneurysms of the carotid or its branches are treated by proximal ligation in stages. If feasible, extirpation or obliteration is carried out. Ligation of the common carotid in vertebral artery aneurysms makes them worse. Innominate aneurysms are difficult to treat. The surrounding adhesions make the procedure dangerous and, at times, forbidding. The Matas operation is not useful here. Ligature and removal have been done in only three reported cases, and they were all successful. "Triple" ligation is curative. This consists of proximal ligation of the innominate with ligation of the carotid and subclavian. The carotid should be ligated first to test cerebral circulation, promote collateral development, and prevent subsequent cerebral embolism or propagating thrombosis following operation on the aneurysm in which cerebral complications are common. Distal ligations alone have resulted in cures. Internal mammary and intercostal arteries if injured may form false aneuryms presenting subpleurally or intrapleurally. Syphilitic aneurysms of the aorta and other large vessels have been successfully treated by lifting the pleura or peritoneum covering most of the surface of the aneurysm with Polythene film or injecting the fibroblastic substance of Polythene-dicetyl phosphate around the aneurysm.

Moore, in 1864, introduced the method of producing a clot in the aneurysm by means of wire introduced within the sac. Corradi, in 1875, suggested the use of silver wire introduced through a hollow needle. The protruding end of the bore wire was then connected to the positive pole and the negative electrode was applied to the skin in the neighborhood and a galvanic current passed. Recently this method has been revived for use in large syphilitic and arteriosclerotic aneurysms. Wire used is fine (34 gauge B. & S.), insulated coin silver or 30- gauge stainless steel. This in itself will produce clotting. Blakemore advocates the use of silver wire in 10-meter segments heated to 80° C. by using approximately 100 volts of direct current. "Brimful" clotting is dependent on an adequate and efficient clot-stimulating surface to the passing blood. To accomplish this a means of measuring blood flow in the aneurysm is necessary to know how much wire to use. This is measured by noting the number of amperes required to raise the temperature of the wire 15° C. When one or more segments of wire, well distributed within a saccular aneurysm, requires only 3 amperes to heat the wire to 80° C., mass clotting of the aneurysm takes place. Unheated wire produces gradual occlusion and has been used proximal to the origin of the aneurysm, whereas heated, insulated wire produces quick coagulation, thereby producing endoarterial occlusion and electrothermic coagulation. Although wire was originally introduced blindly with the aid of the fluoroscope through a small nick in the skin, this method has been

If the pulse could be obtained distally or if the extremity remained pink and warm, collaterals were ample. This test may be misleading if pressure is made upon a principal collateral which may be very close to the aneurysm.

Oscillometric readings may help; elevation of the extremity 30 to 40 degrees may be of value. If it remains pink, circulation is adequate; if cyanosis occurs, it is questionable; and if white, it is inadequate as a rule. At the time of operation the best test is bleeding from the distal artery or pulsation after ligation of the proximal portion (Henle-Coenen phenomenon).

The treatment of aneurysm is old. Compression, injection of sclerosing agents, and ligations were used. Antyllus (fourth century A.D.) ligated above and below the sac, opened it, and packed it; Anel (1710) ligated the proximal artery close to the sac; Hunter (1760) tied the femoral artery high in Hunter's canal. All of these procedures failed because of infection, hemorrhage, gangrene, or recurrence. Brasdor (1760) advised ligation distal to the sac. This may be successful if there are no branches between the aneurysm and the distal ligation and is therefore used occasionally in the treatment of aortic, innominate, iliac, carotid, and subclavian aneurysms.

Matas, in 1888, advised opening the sac and occluding all openings and then obliterating it by successive layers of sutures—obliterative endoaneurysmorrhaphy. A sacculated aneurysm may be treated by restorative endoaneurysmorrhaphy; that is, opening of the sac, closure of the communicating aperture, and imbrication of the sac, permitting the arterial lumen to remain patent. If collateral circulation is poor, reconstructive endoaneurysmorrhaphy may be tried—this consists of obliteration of openings into the sac and the main arterial entrance and exit and imbrication around a tube which is removed before final closure. Even though thrombosis ultimately occurs here, collaterals will have been stimulated by the procedure. Matas' operation is easy and safe. With a tourniquet in place or control by proximal and distal tape, the sac is opened and the laminated clot removed; surrounding structures are not molested. This is important because of perivascular adhesions. If the sac is dissected loose, nerves, collateral vessels, and veins may be injured.

Wherever feasible, proximal and distal ligation with excision of the sac is preferred. If the vessel wall is normal, as in traumatic aneurysm, excision may be followed by direct end-to-end anastomosis. Obviously this is most desirable. Large aneurysmal sacs may be aided in their obliteration by using pedicled or free muscle transplants sewed over the inside openings. Muscle adheres to intima by the development of a proliferative endarteritis and recanalization does not occur. This is done in addition to ligation whenever the latter is feasible. In cases where no

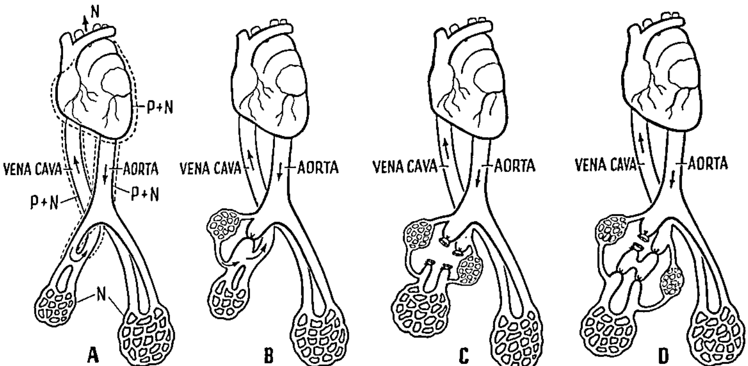

Fig. 178.—Arteriovenous fistula. Diagrams illustrating arteriovenous fistula and its effects. (Redrawn from Holman: Ann. Surg. 122: 210, 1945.) *A*. Shows the fistula and the effects of the parasitic circulation as a result of which there is a dilation of the circulatory bed to transport the increased blood volume. *P*. Parasitic circulation. *N*. Normal circulation. *B*. The effect of ligation proximal to the fistula. Due to the lesser resistance of the fistula, the blood goes back without circulating through the peripheral vascular bed, thereby causing gangrene. *C*. Operation by which the fistula is entirely excised. Ligation of the artery and vein and division proximally and distally. This is the operation of choice. *D*. In cases where this is not possible, an alternative method may be employed whereby there is proximal ligation and division of the artery and ligation of the distal portion of the artery, and ligation of the vein proximally and distally. This quadruple ligation has the same effect as extirpation except that it must be made impossible for recanalization to occur. After quadruple ligation, some form of endoaneurysmorrhaphy may be done whereby the sacs may be imbricated by sutures. The difficulty with the operation of choice is that very often there is danger of injury to important nerves and contiguous structures when the entire arteriovenous fistula in excised.

abandoned except for those aneurysms very close to the skin. It is preferable to open the thorax or abdomen instead of blindly using a trocar through the back in the latter or through the anterior chest in the former. Hydrolyzed polyvinyl acetate and other compounds have been used in the wire for their tissue-irritating effects.

We have recently employed dicetyl phosphate which is the active ingredient on Polythene film which produces fibrosis. This substance has been injected in dogs beneath the mediastinal pleura and peritoneum surrounding the thoracic and abdominal aorta. Dense fibrosis ensues.

Arteriovenous Anastomoses, Aneurysm, and Fistula.—In some regions arterioles communicate with venules; for example, skin of palm of hand and terminal phalanges, the nail bed, skin of lips, nose, tongue, eyelids, and tip of tongue. This is an addition to the capillary communication.

The placenta through the chorionic villi is an example of a physiological arteriovenous fistula; it is true in utero and produces more symptoms as a result of the shunt if the pregnancy is intra-abdominal. Congenital anomalies such as a patent ductus arteriosus or large hemangiomas, particularly in the liver, are examples of a direct communication between artery and vein. Great hyperplasia and hypertrophy of vascular organs constitute another type of arteriovenous fistula; this phenomenon may explain some of the symptoms in exophthalmic goiter. (Chapter 22.)

The term arteriovenous aneurysm is used to describe an arteriovenous fistula with a surrounding sac. Congenital arteriovenous fistulae are also termed pulsating angioma, cirsoid aneurysm (which may be traumatic), simple angioma, varicose aneurysm, cavernous angioma, aneurysm by anastomosis, arteriovenous varix, aneurysm or angioma arteriole serpentina, plexiform angioma, and angioma racemosum.

The etiology may be congenital or acquired. In the latter a penetrating wound by a knife or bullet is the usual cause; where shotgun shells are used, there may be more than one communication. We have had a case with three openings due to buckshot. Bacteria may be the cause, as by embolism with erosion.

Perhaps the most interesting, though rare, malformation is a traumatic connection between an artery and vein. Blood is shunted across from the former to the latter, forcing the unprepared vein to carry arterial blood. If superficial, a pulsating mass and systolic thrill are felt. Also a systolic bruit can be heard. If the carotid artery and jugular vein are involved, the patient can hear the "swish." Great enlargement of the part occurs, with cyanosis due to passive congestion (and the accumulation of reduced hemoglobin) and edema, with resultant fibrosis, eczema, ulceration, and even gangrene. The extremity usually is larger and longer and warmer than the other, unilateral varicose veins are present, and there is chronic venous insufficiency. The distinctive features of a

substance originating in ischemic tissues (Lewis) or due to the theory that blood supply increases with "tissue needs" (Reid). If the distal artery and its branches are patent, collaterals form due to retrograde flow. Moreover, collaterals may be prevented from forming by ligating the artery just distal to the fistula, leaving no branches between the fistula and the site of ligation. The application of a band on the artery proximal to the fistula prevents dilation of the artery by limiting the volume flow of blood through it. The application of a band on the vein proximal to the fistula causes great edema.

End pressure in an artery is determined by peripheral resistance. The greater the end pressure, the greater will be the lateral pressure which is directed into the branches of the vessel. Since end pressure in the artery of an arteriovenous fistula is greater than that at the site of the fistula, blood will be diverted into the vein where resistance is low as compared to the capillary bed distal to the fistula. Moreover, the distal arteriolar and capillary beds will have a great reduction in pressure as compared with the arteriolar and capillary bed proximal to the fistula. Due to this low pressure, blood will be attracted from the proximal to the distal arteriolar and capillary beds, resulting in an increased flow through the corresponding collateral vessels which open up and become dilated in response to this increased flow.

6. Occasionally the artery distal to the fistula is dilated. This is due to an occlusion of the proximal artery by thrombosis with fibrous tissue healing. The site of diminished peripheral resistance attracts blood from all collaterals which in turn connect with branches of the artery distal to the fistula. The resulting, greatly increased volume of blood flowing back through the distal artery causes its dilation.

7. Closing the fistula produces dilatation of the already dilated heart, the aorta, and all of the vascular system as shown by roentgenological kymography (Holman). The dilated aorta stimulates depressor vagus fibers, causing a slowing of the pulse. Perhaps this is augmented by the carotid sinus reflex as well. Atropine eliminates this response showing its vagus origin.

8. Elimination of the fistula permanently is followed by a reduction in blood volume through loss of plasma as shown by increased urinary output and hemoconcentration for a brief period. This results in a decrease in the size of the heart except for the slight hypertrophy which took place during the life of the fistula.

Treatment.—The treatment of arteriovenous fistula may be an emergency. If hemorrhage continues after bed rest and pressure bandage, immediate ligation and division of the vein is done to avoid the danger of embolism from air or thrombus and to improve collateral circulation. The hole in the artery is then closed either by lateral suture or resection and suture. If suture is impossible, then ligation and division of the artery and vein above and below must be done. The blood

fistula as compared with an aneurysm are a continuous thrill and bruit exaggerated during systole; slowing of pulse and rise in blood pressure on digital closure of the proximal artery or fistula; high oxygen content of venous blood. As a result of lowered peripheral resistance and increased venous return, there is cardiac acceleration. The heart must pump an increased volume of blood and therefore dilates and hypertrophies.

Pronounced circulatory effects often follow with dyspnea, tachycardia, palpation, syncope, and even death. This remarkable lesion has led to some very interesting observations on the altered physiology which are explained by Holman as due chiefly to the introduction of a new circulation parasitic upon the normal circulation. A study of available experimental and clinical observations leads to the following deductions:

1. There are two circulations—the normal and the parasitic. The latter differs from the former in that it lacks a capillary bed and substitutes an opening between artery and vein. Each system needs blood and gets it. When the parasitic circulation attracts more than the normal, the patient dies.

2. The effect of this blood diversion is like that of neurogenic shock with (1) a lowering of blood pressure, (2) with a lowering of blood pressure, accelerated pulse, temporary reduction in size of the heart and the artery proximal to the fistula.

3. A redistribution of blood and fluid from the spleen, liver, and tissue spaces soon occurs which restores the pulse and blood pressure to normal. Due to this accretion of fluid and blood there is an increase in blood volume which, when redistribution is complete, circulates through the normal and parasitic systems.

4. Dilatation of the heart and the circulatory bed through which the short-circuited blood passes results due to the increased blood volume. The reverse is true in patients with shock due to loss of blood volumes—that is, the heart and vessels decrease in size. Dilation of the fistulous circuit is due to the fact that there is less peripheral resistance in these vessels which do not go through a capillary bed; and since blood flows through the path of less resistance, more and more blood from the rest of the circulation occupies this parasitic circulation. This diminished blood volume in the rest of the circulation attracts more fluid and blood into fill the vascular tree. Thus there is a gradual but progressive increase in total blood volume.

5. The determining factor in this gradual dilatation is the extent of the difference in peripheral resistances in the two circuits. This, in turn, is determined by (1) the size of the fistula, (2) its proximity to the heart—the nearer the heart the greater the discrepancy in peripheral resistances and vice versa, and (3) amount and firmness of fibrous tissue around the fistula. Collaterals were thought to form due to a chemical

Many operations have been tried and have failed: (1) Ligation of the proximal artery will cause more blood to pour through the fistula and less to go through the peripheral capillary bed as previously explained, causing gangrene of the extremity. (2) Ligation of artery and vein proximally does not cure because collaterals will supply blood to the fistula, although this operation may be used as a preliminary step to extirpation. (3) Ligation of the large veins above and below will simply cause collaterals to fill up the dilated venous system with blood and deprive peripheral capillaries at the same time, increasing venous varicosities. (4) Ligations proximal and distal to the vein and artery are useful as a preliminary—recurrences do occur due to reopening of the proximal artery.

Many operations have been found useful: (1) Transvenous or transsaccular closure (Matas-Bickham). The vein is opened under tourniquet control, the opening or openings in the artery closed, and the vein ligated above and below the rent and its wall used to reinforce the suture line in the artery. (2) Ligation of the artery and vein proximal and distal to the fistula *with division of the proximal artery* where dissections are impossible due to dense fibrous adhesions to nerves. (3) The same as (2) with endoaneurysmorrhaphy, especially if arteriovenous aneurysm is present. (4). The best procedure is ligation of the artery and vein proximally and distally and excision of the fistula. (5) Rarely (4) may be done with anastomosis of the resected artery, thus assuring ample blood supply. This is necessary because in some cases in spite of ample collateral circulation the extremity shows some atrophy and disability with vasomotor changes after excision. (6) Arteriovenous fistulae of the face and scalp have intracranial origin in about 75 per cent of the cases and are usually congenital. The middle meningeal artery on one or both sides provides the arterial supply. Rarely the external carotid or its branches provides the main arterial branch. Careful x-ray study and neurological examination should be done in all cases because the aneurysms or fistulae may involve the brain as well as the dura. The best *treatment* is excision of the primary angiomatous mass. If this is in the dura, the vessels penetrating the bone should be waxed after the scalp has been stripped from the affected area. Sometimes dural varices must be exposed and ligated or coagulated and the middle meningeal artery (one or both) tied. Ligation of the external carotid may be necessary or both external and internal may be required. If in doubt one should expose the common carotid and place a tape around it so that he has control—we have felt that ligation of the common carotid is less dangerous than ligation of the internal carotid. Some authorities advise ligation of the internal jugular vein at the same time (Makins).

The closure of an arteriovenous fistula may raise the systolic and diastolic pressure to such a degree that acute cardiac failure may result. In this event the blood pressure would fall and the pulse rate rise. Vene-

pressure must be kept up by antishock measures—chiefly, repeated massive blood transfusions. Sympathectomy (chemical or surgical) has been advocated by many. Recent studies from extensive war experience do not substantiate its value in all cases.

In the presence of infection or a small wound or one without excessive bleeding, operation may be deferred five to six months to allow for collaterals to form and in the hope that a small fistula may close spontaneously; also the danger of infection will be less and dissections will be easier.

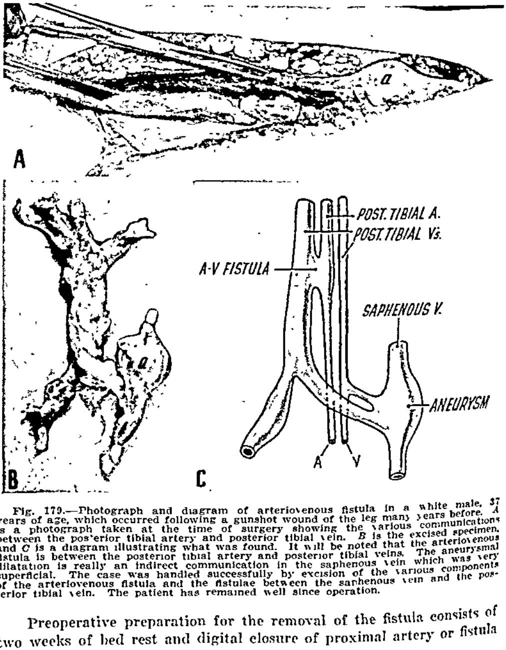

Fig. 179.—Photograph and diagram of arteriovenous fistula in a white male, 37 years of age, which occurred following a gunshot wound of the leg many years before. *A* is a photograph taken at the time of surgery showing the various communications between the posterior tibial artery and posterior tibial vein. *B* is the excised specimen, and *C* is a diagram illustrating what was found. It will be noted that the arteriovenous fistula is between the posterior tibial artery and posterior tibial veins. The aneurysmal dilatation is really an indirect communication in the saphenous vein which was very superficial. The case was handled successfully by excision of the various components of the arteriovenous fistula and the fistulae between the saphenous vein and the posterior tibial vein. The patient has remained well since operation.

Preoperative preparation for the removal of the fistula consists of two weeks of bed rest and digital closure of proximal artery or fistula for one-half hour every two hours.

The thin-walled vessels and sinusoids may be very large and pulsating (cirsoid aneurysm). Cavernous hemangioma may be found in any organ or structure in the body. We have seen them on the face, scalp, neck, buttocks, oral mucous membrane, liver, bone, synovial membrane, muscles of the legs, stomach, intestine, rectum, and broad ligament. The treatment is ligation of the vessels and surgical excision in stages, if large, followed by skin graft if on the skin. If its removal impairs the blood supply to an organ, the organ may have to be removed. For the superficial varieties, electrocoagulation, radium, x-ray, and sclerosing solution have been advocated. Hemangiomas may disappear due to spontaneous

Fig. 181.—Angioma racemosum (cirsoid aneurysm). The patient is a woman aged 24 years. In an automobile accident nine years previously she was cut with glass in the right temporal region. The present condition began six months later and gradually increased in size. An arteriovenous fistula was found between the temporal artery and the vein. This was cured by ligation of the external carotid and excision of the dilated vessels. Ligation of the common carotid artery may be fatal or may cause hemiplegia; therefore, the artery is occluded in stages.

complications such as thrombophlebitis; hematoma due to trauma or spontaneous; erysipelas, nonspecific infection. Some disappear without treatment or complication. Therefore, they are watched and if growth is progressive they are removed before they become very large.

2. Racemose or cirsoid aneurysm resembles an hemangioma, which it may be. This has already been discussed under arteriovenous fistula.

3. Diffuse systemic hemangioma is like a combined capillary and cavernous type involving a large area like an entire extremity. There

section would help by reducing blood volume temporarily to allow for readjustment. Following the operative closure of the fistula the patient's activities should be restricted for six to eight weeks.

TUMORS OF BLOOD VESSELS

Under the term tumor may be included various types of swellings, abnormalities, and neoplasms which involve blood vessels or endothelium. These include the following entities:

1. Hemangiomas are benign tumors, congenital in origin, made up of newly formed blood vessels which grow as do newly formed blood vessels in granulation tissue; namely, solid cords of endothelial cells which become canalized and communicate with parent vessels. There are two kinds of hemangioma (nevus or birthmark)—*capillary* and *cavernous*.

Fig. 180.—Cavernous hemangioma of the face The distribution is roughly that of the ophthalmic and maxillary divisions of the trigeminal nerve.

The flat "port-wine" marks on the face that blanch on pressure represent the *capillary* type. Sometimes they cover one-half of the child's face; often they are only the size of a dime or quarter; they are commonly called nevi (birthmarks). They are due to an abnormal number of small capillaries, which are known to follow roughly the course of nerves. The type called strawberry nevus is more circumscribed and slightly elevated. They are sometimes found with fibromas (hemangiofibroma) or fatty tumors (hemangiolipomas). Hemangiolymphangiomas are seen occasionally. The *treatment* is radium, x-ray, or carbon dioxide "snow."

A cavernous hemangioma (nevus cavernosus, cavernoma) is a large collection of venules and arterioles. It is elevated due to connective tissue about the vessels, and usually has a principal artery and vein.

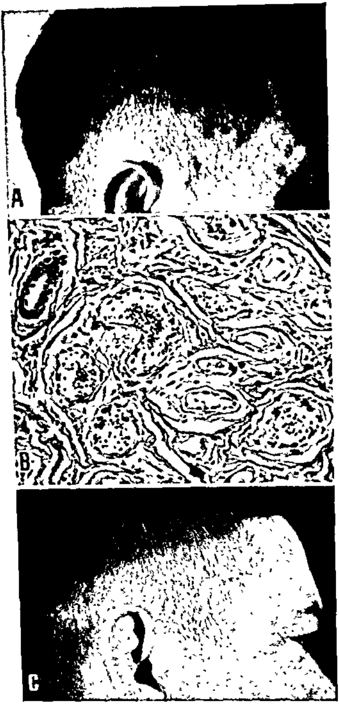

Fig. 183.—Hemangioendothelioma. *A*. Clinical photograph of the patient prior to operation. E. M., forty-five years previously, complained of a swelling in front of the ear and many smaller tumor masses throughout the right portion of the scalp. This proved to be an aneurysm of the temporal artery and multiple endotheliomas of the branches of the temporal artery. *B*. Photomicrograph of sections of the excised tissue (medium power) showing blood vessels of capillary size and of somewhat larger caliber. Note the thickened and edematous walls, the large cells, and occasional mitotic figures. (Case of Dr. H. Pandolfo, Dr. D. Kelly, and Dr. J. Dalton.) *C*. Postoperative clinical photograph after the aneurysm had been removed and the endotheliomas excised. In order to avoid complications, a temporary ligature was placed around the common carotid artery because it was feared that there might be intracranial connections. This did not prove to be the case.

is tissue hypertrophy due to the abnormal blood supply. Sometimes there is great shrinkage on elevation, revealing congenital absence of bones or deformities. Treatment is unsatisfactory. Ligation of the greater and lesser saphenous veins with retrograde injection may be helpful but is not curative as a rule. Excision in sections with skin graft is best.

Fig. 182.—Diffuse systemic hemangioma (combined capillary and cavernous types) of the entire right lower extremity. The child was 2 years old on admission to the hospital. The lesion was present at birth and had grown rapidly. Treatment with x-ray was not successful. X-ray examination showed no bone involvement. Stage operations were planned to remove small areas at a time followed by immediate skin grafts. The child's parents would not consent to surgery.

4. Hemangioendothelioma is a malignant neoplasm with proliferation of endothelial cells. Hemangiosarcomas have, in addition to vascular tissue, fibroblastic connective tissue. Angioblastic or hypertrophic hemangioma are solid elevated masses of endothelial cells with a few patent vessels. These do not metastasize but do tend to recur locally after removal. Metastasizing hemangioma is very rare; it has been re-

Fig. 183.—Hemangioendothelioma. *A.* Clinical photograph of the patient prior to operation. E. M., forty-five years previously, complained of a swelling in front of the ear and many smaller tumor masses throughout the right portion of the scalp. This proved to be an aneurysm of the temporal artery and multiple endotheliomas of the branches of the temporal artery. *B.* Photomicrograph of sections of the excised tissue (medium power) showing blood vessels of capillary size and of somewhat larger caliber. Note the thickened and edematous walls, the large cells, and occasional mitotic figures (Case of Dr H. Pandolfo, Dr. D. Kelly, and Dr. J. Dalton.) *C.* Postoperative clinical photograph after the aneurysm had been removed and the endotheliomas excised. In order to avoid complications, a temporary ligature was placed around the common carotid artery because it was feared that there might be intracranial connections. This did not prove to be the case

ported in the breast with metastases to the lung, yet it appears microscopically *as a benign tumor. Hemangioendothelioma* of bone (Ewing's tumor) is a special type seen in the shaft of long bones in young individuals. Usually hemangioendotheliomas *grow slowly and metastasize* late—some are very malignant. Treatment consists of wide excision if possible, x-ray treatment if not, or perhaps both may be indicated. A leg may have to be amputated if x-ray treatment fails.

5. Telangiectasis is an acquired dilatation of capillaries and small venules. (1) Spider nevus (nevus araneus) is a very small lesion with a pinhead size and radiating tiny capillaries. (2) Senile ectasia (senile vascular nevus) is a raised lesion slightly larger than the spider nevus. These may be removed by fulguration. (3) Hereditary hemorrhagic *telangiectasia (Rendu-Osler-Weber's syndrome) is characterized* by multiple telangiectatic lesions of the skin and mucous membranes with a tendency to bleed. The disease is familial and is said to be inherited

Fig. 184.—*Macroglossia due to hemangioma.* The condition improved under radium treatment.

as a dominant characteristic. The lesions are flat and are red or purple and blanch on pressure from a glass slide. Due to the frequent hemorrhages, patients become anemic. The lesions may be distinguished from petechiae or purpuric spots by their tendency to blanch on pressure and their peculiar distribution (nasal and oral mucous membrane, hands and face); from *hemophilia* by the prolonged *coagulation* time in this disease; from thrombocytopenic purpura by the low platelet count, prolonged bleeding time, and bleeding from gastrointestinal tract more often in purpura; from aplastic anemia by a decrease in platelets, increase *in* bleeding time, and clot retraction time in aplastic anemia; from acute leucemia by leucocyte differential and total counts and by *splenomegaly* in acute leucemia. The *treatment* consists in stopping bleeding by pressure or *fulguration of the lesion and repeated* transfusions. (4) Pulsating telangiectasis resembles spider nevi which pulsate. They are probably minute hemangiomas and seem to be associated with liver diseases. They may be removed by fulguration.

VEINS

A dilatation of the superficial veins may occur as a result of arteriovenous fistula and hemangiomas, conditions which we have discussed. More commonly there is some obstruction to the venous return either due to cardiac failure or some impediment to the flow of blood back to the heart; in the latter instance the veins distal to the obstruction will be dilated, and, in addition, many new or collateral veins will appear which are also very large and unnatural. Perhaps even more often there is a congenital defect in the valves of veins which permits them to dilate and become tortuous; these usually appear in the legs and are known as varicose veins.

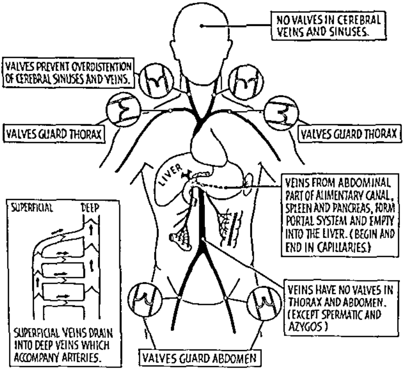

Fig. 185.—Diagram illustrating the valves in veins. There are practically none in the abdominal and thoracic veins. The pressure in the thoracic veins, though low, is greater than the pressure in the thoracic cavity (which is negative), permitting blood to flow into the right auricle. Variations in position and pressures within the thorax and abdomen may thus affect the venous return Insert shows flow of blood from superficial to deep veins, with valves preventing reflux.

Varicose Veins

The latin *varus* means crooked and *varicosus* means dilated or enlarged vein. *Saphenous* comes from the Greek, meaning manifest. Varicose veins are dilated, crooked veins usually seen in the saphenous veins of the legs.

There is a deep set of veins lying in the muscles and a superficial set lying under the skin. In the leg the deep vein is the femoral vein, and the superficial veins are the great and lesser saphenous veins. The

deep veins are surrounded and supported by muscles. But the long or great saphenous vein lies unsupported just beneath the skin. Blood flows from deep to superficial veins below the ankle, but from superficial to deep through the communicating vessels above.

Pathogenesis.—It is easy to understand the development of varicosities secondary to obstruction of the deep veins. Here they become dilated while acting in the capacity of collaterals. In iliofemoral thrombophlebitis the valves of the femoral vein may be permanently rendered incompetent by destruction and fibrosis. Extrinsic pressure at the iliofemoral junction may act in the same way. However, pressure within the abdomen due to pregnancy, tumors, and ascites will usually not result in varicosities if the valves are competent. Thus we see that the most important factors in the development of varicose veins is the condition of the valves. Incompetency of the valves may be present in the long saphenous (usually) or lesser saphenous, the perforating veins, or all of the superficial and communicating veins and may be due to: (1) Congenital absence. The external iliac and femoral veins proximal to the saphenous show no valves in about 33 per cent of all people. (2) Hereditary weakness in vein walls and valves which allows for dilation and incompetent valves from any cause which increases intralumenal pressure; namely, orthostatism, obesity, pregnancy, abdominal tumors, ascites, abdominal aneurysms. (3) Hereditary weakness which allows for phlebectasia due to decrease in extrinsic support as seen in thin, old, and emaciated men, in persons after prolonged bed rest, after plaster casts on the legs. From any of the aforementioned causes there results a series of pathological changes which consist of dilatation, elongation, tortuosity, fibrosis with variation in thickness, loss of elasticity due to fibrosis and stretching, incompetency of valves due to their atrophy. (4) Incompetency of valves in the communicating veins. Since the pressure in the deep veins is higher, blood flows into and stops in the saphenous.

If the saphenous vein is weak or diseased or if its valves are destroyed, it becomes enormously enlarged and tortuous because the blood gravitates down (in a reverse direction to the normal flow) when the patient stands. It is perhaps more correct to say that there is an inherent or congenital weakness in the varicosed vein which is aggravated by occupations which require long hours of standing. The column of blood extending from the right auricle to the ankle causes dilatation and sacculation of the vein, which may lead to complications, such as edema, ulcer, rupture of the vein, thrombophlebitis, eczema, and all manifestations of venous insufficiency with stasis.

Actually a reverse flow is rare, and if present at all it must occur in severe late cases with the patient standing still. In most cases there is probably stasis or very slow movement toward the heart which is not fast enough to carry away the capillary inflow. Active motion speeds up this re-

turn to some extent and elevation makes it normal. Blood pools to some degree in most people—soldiers standing at attention frequently faint. Experiments in which persons stand in a tub of water for a period of time show a rise in the level of the water due to swelling of the feet and lower legs. Patients with large capacious varicose veins may faint due to the enormous quantity of blood which may be trapped, thereby reducing blood volume. We have seen patients with varicose veins who presented symptoms of lightheadedness or sense of goneness after standing for several

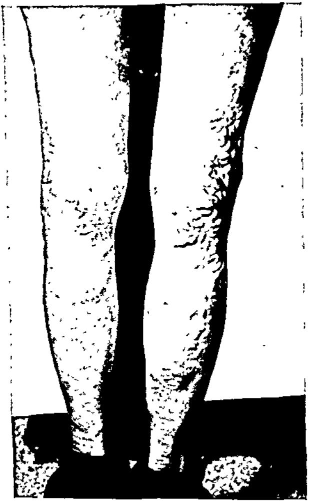

Fig. 186.—Varicose veins of both legs, with involvement of the greater and lesser saphenous.

hours. Walking or flexion of the legs helps, but unless they assume the recumbent position, collapse follows. Since the syndrome is transient, it must be due to temporary pooling with reduction of blood volume and vasoconstriction, and cardioacceleration follows with more blood pumped into the large varicosities then collapse due to aortic or carotid sinus reflexes. This same syndrome occurs occasionally in acute venous thrombosis.

Most observers have found an increase in venous pressure in varicose veins while patients are standing and normal pressure while recumbent. Some have found the reverse to be true and have felt that, as in arteriovenous fistula, there is an increase in blood volume in patients with large varicosities. When the patient lies down, an increase in circulating blood volume results, increasing venous pressures in the varicose veins which had normal pressures on standing. Arterial blood flow is unaffected in legs with varicose veins. But there is a higher incidence of arteriosclerosis of the leg arteries in men with varicose veins. This difference is not seen in women, who show a higher incidence of varicosities than men.

Pooling of blood leads to anoxia, and the increase in intravenous pressure plus anoxia contribute to the development of phlebosclerosis and intimal damage. Phlebitis and periphlebitis ensue with subsequent damage to the overlying skin, particularly over the most dependent portions of the involved veins.

Stasis with anoxia causes necrosis of tissue, and these tissues with their poor resistance may break down from the slightest injury, with the subsequent formation of a *varicose ulcer*. Healing will not take place because of *edema*, which prevents nutrient material and oxygen from reaching the tissue cells and waste products from being carried away. Stasis ulcer and postphlebitic ulcer are supposed to be special varieties of the lesion due to separate causes. Since the underlying cause is usually the same, the distinction is more academic than real. There is no doubt that ulcers do develop early in the presence of varicose veins, occasionally due to an underlying phlebitis and periphlebitis, resulting in cutaneous induration and ulcer. Really all injuries in the lower legs are slow to heal because a certain degree of stasis is present even in normal veins.

Competency of Veins.—Various tests are used to show the competency of veins. The Trendelenburg test simply occludes the long saphenous by a bandage with the patient recumbent. He then stands and the pressure is released. The incompetent veins fill from above down, with a sudden drop. The double Trendelenburg is used to determine the competency of the communicating vessels. With the above bandage in place, the saphenous vein will normally fill from below in about thirty seconds. If the communicating vessels are incompetent, this time is greatly reduced. Sometimes the saphenous vein is competent, the communicatnig vessels are not. In such instances the first Trendelenburg will be "negatve" and the double Trendelenburg will show that the saphenous fills no more rapidly even if the bandage is suddenly removed. Perhaps the most practical test for incompetent deep veins is the use of an Ace bandage or rubber stocking. Since patients with incompetent deep veins need the superficial veins as an aid in the return flow, any obstruction to them causes pain and swelling in the foot. Another simple manner to determine the competency of the deep veins is as follows: *A*

band is placed above the thigh just tight enough to occlude the superficial veins while the patient is standing. With the band in place, the patient is asked to lie down. If the deep veins are open, blood will leave the leg and the superficial veins will collapse. If not, they will remain distended. Another useful test is the one described by *Perthes*. A tourniquet is applied to the thigh tight enough to occlude the long saphenous but not the femoral. The patient is asked to walk rapidly. This causes the saphenous veins to fill with blood quickly. If the varices disappear rapidly on walking, the communicating veins are competent but the saphenous is incompetent. If the veins remain distended on walking, then both saphenous and communicating venous valves are inadequate. If, in addition, there is severe pain and the varices become larger and the foot and ankle swells, the deep veins are probably obstructed. By using this test at different levels up the leg, segmental thrombosis of the deep vein may be detected which might otherwise be missed due to blood circuiting around the obstruction. The Pratt test helps to locate the exact position of incompetent communicating veins. A tourniquet is placed around the thigh with the leg elevated tight enough to constrict the saphenous; an elastic bandage is then wrapped from the toes to the tourniquet. The patient stands, and as the bandage is unrolled, the bulging incompetent veins are apparent and a mark is made on the skin with an indelible pencil.

Treatment.—Patients with varicose veins demand treatment usually because of (1) general symptoms, (2) local complications, and (3) cosmetic reasons. Often patients will ask for instructions to prevent the formation of varicose veins since they know it to be a familial tendency. This is especially true in nurses, dentists, and others who know that orthostatic effects may hasten the development of phlebectasia. Obviously there is no prevention in those cases due to inherent weakness or congenital absence of venous valves. Avoidance of tight garters, long standing, and infections is desirable. Really the prevention of varicosities, except those secondary to obstruction, is a difficult problem.

Surgical intervention is the desirable form of treatment but when contraindications to surgery exist, other forms of treatment, even though palliative, may be instituted. Excision is contraindicated in arterial disease (thromboangiitis obliterans, arteriosclerosis, Raynaud's disease), in thrombophlebitis of the femoral vein, in cardiac decompensation, and when there is a great increase in intra-abdominal pressure from tumor or ascites; also in any severe infection in the leg (cellulitis or lymphangitis), advanced malignant disease, severe renal disease, uncontrolled diabetes, general infection until recovery is complete, active tuberculosis, and severe blood dyscrasia.

Most patients have some local complication of varicose veins and therefore the treatment of ulcer should be discussed along with the management of the varicosities.

The treatment of a varicose ulcer is to remove its cause: the stasis due to incompetent veins. Any measure directed against this will ultimately effect a cure. The idea is to send the blood back to the heart through the deep veins which are competent. This may be accomplished by elevation of the leg, elastic bandage, Unna's paste boots, or surgical excision of the useless veins. However, the surgeon will make sure that the deep veins are competent, that there is no intra-abdominal growth, and that no arterial disease is present before doing the latter. Once venous stasis is relieved, the ulcer will usually heal. The entire vein may be removed by subcutaneous tunneling. Most important is its interruption at the saphenous opening. This must be done by careful dissec-

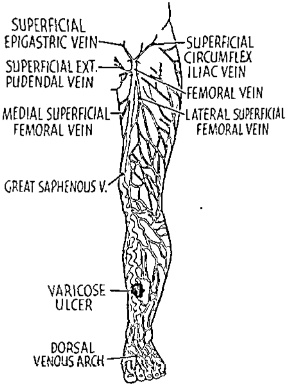

Fig. 187.—Diagram illustrating the great saphenous vein and its branches and a varicose ulcer in the usual location. This arrangement is by no means constant. Many variations occur. To break up the column of stagnant blood the saphenous vein must be divided in the saphenous opening, where it joins the femoral. To prevent recurrence, its five branches must also be divided The distal portion of the vein may be removed by "tunneling," or through small incisions along its course. It may be obliterated by the retrograde injection of sclerosing chemicals. However this method may be followed by deep thrombophlebitis. It is better to inject the sclerosing agent later after the effects of ligation have been determined.

tion of the long saphenous at its junction with the femoral in the saphenous opening, thereby interrupting the column of blood. In addition, the four branches are divided between ligatures, or excised. This procedure prevents the reformation of varicosities. Following the removal of the terminal section of the saphenous vein, the remaining varicosities are removed or stripped through short incisions. The Schede operation interrupts all branches by a circular incision down to the deep fascia which extends around the circumference of the leg. Percutaneous

ligation is useful in the treatment of small varicosities and may be used in conjunction with the above in severe cases. Recently much has been written about the injection method of treatment. Irritating solutions such as sodium morrhuate, 5 per cent, with benzyl alcohol, sodium ricinoleate, 3½ per cent, 50 per cent glucose, quinine, and urea hydrochloride have been used. This method is only temporary and is, in addition, painful and dangerous but will be successful in conjunction with ligation. The varicose ulcer is treated by applying a small rubber sponge on the gauze-covered ulcer and holding the sponge in place by an elastic bandage. This keeps the blood and serum out of the area until healing has occurred. Ointments and antiseptics have little value. The ulcer extends down to the deep fascia, which is usually not involved. Excision of the ulcer down to the fascia with subsequent skin graft may be necessary if extreme fibrosis is present.

Notes on Technique.—Extreme variations exist in the anatomical distribution of the tributaries of the saphena magna; therefore, each case demands wide exposure and careful search. All operations are done under local anesthesia. The best guide is the femoral artery—the vein lies medial. The incision is made just below and parallel with the inguinal ligament. The external or superficial pudendal artery is a guide to the saphenofemoral junction. Retrograde injection is not done because of the danger of (1) venospasm severe enough to cause reflux into deep veins through incompetent communicative veins, (2) arterial spasm which in arterial disease may finish the occlusion, producing gangrene, (3) sensitivity to the sclerosing agent. The lesser saphenous is ligated and divided as it enters the popliteal, if it is involved. Patients must be seen at six-month intervals—if new bulges occur, they should be removed or injected. Prognosis: usually good—not favorable in the obese or extremely thin and old.

Varicose veins are seen elsewhere in the body besides the legs. A few instances may be menitoned here. The usual cause is venous obstruction or arteriovenous fistula. *Prominent chest and arm veins* may be due to compression or partial obstruction of the subclavian between the clavicle and first rib anterior to the scalene tubercle. Decompression may be done Obstruction of the superior vena cava causes edema of the face and neck which is aggravated on recumbency and is better on arising. Collateral circulation is by way of the azygos. If the superficial veins of the thorax are occluded, venous pressure rises in the arms; if obstruction is close to the heart, inspiratory filling of neck veins may occur in congestive failure, constrictive pericarditis, and superior vena cava obstruction. The superior vena cava is rarely obstructed by thrombosis; it may be due to phlebitis, external compression due to tumors and cysts, mediastinitis, syphilitic, or tuberculous mediastinitis, aneurysms. Prognosis depends on the cause, Usually collaterals form. Thrombophlebitis rarely affects the axillary vein. It is seen following

severe bacteremia, surgical procedures, or intravenous injections by infected or hypertonic solutions. Sometimes a severe injury in or near the axilla may cause it. Occasionally it is seen in severe hemoconcentration from burns and other causes; also in polycythemia vera. *Esophageal varices* associated with Banti's syndrome, thrombosis of the coronary or portal vein, and atrophic cirrhosis may become very large and rupture, causing a fatal hemorrhage. Treatment of esophageal varices may be described under the following heads: (1) Direct attack includes obliteration by excision of the varices outside or inside the esophagus or by injection of sclerosing agents outside the esophagus or within the veins, or by their removal by resection of the lower esophagus and cardiac end of the stomach or the entire stomach. (2) Indirect attack attempts to decrease their size by lessening the amount of blood they carry. This is accomplished through splenic artery ligation or anastomosis between the portal and systemic venous circulations creating a shunt. Thus portal hypertension may be relieved by an Eck fistula, that is, portacaval anastomosis; also by anastomosis between the splenic vein and left renal vein after splenectomy but not nephrectomy and between the mesenterics and the vena cava or spermatic or ovarian veins (see Chapter 22).

Phlebothrombosis, Phlebitis, and Thrombophlebitis

Sometimes the deep veins are blocked also. It happens in phlebothrombosis and thrombophlebitis. Pathologically and clinically phlebothrombosis is probably the early quiet stage of thrombophlebitis. Etiologically it is the type of thrombophlebitis which occurs without previous inflammatory changes in the wall of a vein. Any foreign body in a vein incites a reaction or phlebitis, and a thrombus is no exception. Therefore a phlebothrombosis soon becomes a thrombophlebitis. The reason for the distinction is the increased probability in phlebothrombosis of a loose fragment from a propagating thrombus which is itself attached flimsily to the wall of the vein, breaking off and being carried to the lungs (See Chapter 5). This is not so apt to occur, in fact, rarely occurs in the later stage of thrombophlebitis when the thrombus is densely adherent. The entire process varies so much in different veins and from different causes that we must conclude that a phlebothrombosis occurs in some cases and remains silent for some time, whereas in others it incites so much reaction that it is a thrombophlebitis from the start—since this is true in all types of inflammation in all tissue, it is also true in veins. In other words, it is the causative factor and the resistance of the vein that determines the types. It should be stated, however, that the silent type is more apt to occur following surgery.

Thrombophlebitis has special names and implies a definite entity in various parts of the body. *Pylephlebitis* or pylethrombophlebitis (*pyle*, gate) are terms used to describe an inflammation and thrombosis with inflammation in the portal vein. Pylethrombosis is a thrombosis of the

portal vein. The inflammations usually follow suppurative diseases of the intestine, particularly appendicitis and diverticulitis. Pyelophlebitis (*pyelo*, a trough) is used to denote an inflammation of the renal vein or its branches.

The cause for *postoperative phlebothrombosis* is not definitely known and is probably a combination of causes which may be summarized under two heads: the increased ability of the blood to clot and the stasis with resultant anoxia of the circulating blood volume. The former has been attributed to (1) a decrease in heparin and an increase in antiheparin constituents because patients are "heparin resistant" for a variable period of time after surgery, (2) hyperprothrombinemia which is present after surgical operations (also after childbirth and coronary occlusion), (3) early decrease, then increased platelet count shortly after surgery, (4) increase in fibrinogen, (5) shift in albumin-globulin ratio in favor of globulin, (6) increase in blood viscosity which favors the agglutination of platelets which normally repel each other. The coagulation of blood is further favored by the postoperative leucocytosis and disintegration of platelets with an increase in thrombokinase. Dehydration and loss of plasma also shorten coagulation time. The slow circulation gives rise to stagnation with stagnant anoxemia. This is seen mostly in the legs in which the circulation normally is slower when immobile. Thus immobility, especially in the obese and those with varicose veins, is particularly conducive to intravenous clotting—in the former due to the obstructive factor which normally slows venous return and in the latter the large and tortuous channels which permit a certain amount of loitering within the varices. If the foregoing factors were all, then the disease should be preventable. But there must be still other causes as yet unknown. Certain it is that (1) phlebothrombosis may occur during the operation and therefore lengthy procedures are conducive, (2) stasis is not the only factor because pelvic operations are prone to be followed by phlebothrombosis in spite of the Trendelenburg position which keeps the veins of the legs empty (is it the local pelvic edema which interferes with venous return following surgery?), (3) phlebothrombosis is rarely seen after breast operations, thyroidectomy, and head operations (can this be explained on early movement, high systolic pressure, and restlessness, respectively?). Phlebitis *and* thrombophlebitis are probably seen most frequently clinically after two conditions: (1) after some acute infections disease, such as pneumonia or typhoid fever, and (2) after operations or abnormal obstetrical deliveries. The *causes* of phlebitis and thrombophlebitis are not definitely known. Among those which may operate are as follows: (1) Factors *outside the vein*, such as trauma during operations or obstetrical deliveries, traumatic injuries, inflammations produced by the streptococcus (cellulitis) or the staphylococcus (carbuncle of the upper lip), inflammation in suppurative appendicitis which may involve the portal vein (pylephlebitis), etc., giving rise to suppurative

thrombophlebitis; also in association with nonsuppurative lesions such as erythema nodosum, tuberculosis, and syphilis. (2) Factors *inside the vein*, such as toxins or infections in diphtheria, pneumonia, malaria, typhoid fever, etc., which produce an *inflammation of the intima*. (3) *Changes in the rate of blood flow*, producing stasis, as during long periods of bed rest (especially in old people) or in spinal anesthesia (long period of muscular inactivity), cardiac disease with failure, ischemia from arterial disease. Since venous flow is dependent in a great measure upon muscular action, there is stagnation due to continued immobility. This results in edema. A vasospasm occurs to counteract this loss of blood volume and the reduced blood pressure which accompanies it. This gives rise to an internal pooling of the blood and a shocklike syndrome. The night pains in the legs of individuals with arteriosclerosis are probably due to the above, with a resultant fall in blood pressure and decreased arterial flow. Thrombophlebitis is accompanied by a spasm of the affected vein and its branches peripheral to the lesion and by an arteriolar spasm as well. (4) *Changes in density of the blood*, as seen in starvation, dehydration, and burns (which produce *anhydremia*), polycythemia vera. (5) *Chemical changes in the blood* such as occur in anoxia, perhaps as a result of smoking, and in toxemias of pregnancy and burns; it may be produced by injection into the veins of a hypertonic solution (such as 50 per cent glucose), which irritates the intima (causes 2), destroys the red blood cells, and increases the density of the blood (cause 4). This may occur in long continuous intravenous drips of isotonic solutions, due to the irritation by the needle. It is also seen after intravenous injection of mercurial diuretics, penicillin, and other drugs. (6) Without any known cause a thrombophlebitis may develop. (7) In association with thromboangiitis obliterans by direct extension. (8) As recurrent idiopathic thrombophlebitis (phlebitis migrans). (9) Venospasm from any cause.

Post-Partum Thrombophlebitis.—After obstetrical deliveries thrombophlebitis with resultant edema is called "milk leg" or *phlegmasia alba dolens* (white and painful leg). It has been called "milk leg" because the early physicians thought it was connected in some way with the "coming in" of milk, since it usually occurred on the fourth or fifth day post partum. *Thrombophlebitis* in varicose veins is painful but not dangerous. It is also not accompanied with edema provided the deep channels are open. Those who inject sclerosing solutions in varicose veins really produce a chemical thrombophlebitis in an attempt to obliterate them. If the saphenous vein is not varicosed, the dangers of embolism are present, as is also the probability of postphlebitic edema.

Pathology.—In addition to the thrombosis and inflammatory reaction in the various coats of the venous wall, three varieties of thrombi have been described: (1) Red thrombi which are homogeneous and resemble post-mortem clots; this type is seen in local inflammation or injury to the vein; (2) white thrombus which consists of fibrin platelets

and leucocytes and usually is the older part; (3) *Mixed type which consists of white thrombus as the head and red thrombus as the tail.* The white thrombus tends to progress distally and may or may not occlude the vein. The red tail develops proximally very quickly and propagates as a result of increased blood coagulability. This tail may become adherent and fill the veins as a firm clot or it may be friable, flapping in the blood stream, giving rise to emboli. A thrombus which is more than *three days old rarely becomes detached. New propagating thrombi may* occur on the old and extend up to the juncture of a large tributary and stop, or others may form as a result of a secondary inflammatory reaction proximally.

The chief danger is the dislodgment of a thrombus which results in pulmonary embolism. Homans states that Kinney, Haynes, and Dexter have introduced a venous catheter into the pulmonary artery in a dog by way of the jugular vein and right heart. By inflation of a balloon at the tip of the catheter there is no change in pulse rate or respiratory rate, the systemic blood pressure, the right ventricular pressure, or the electrocardiogram. Only when infarction follows do signs and symptoms appear. If, however, emboli (lycopodium spores) are introduced into a lobe, acute symptoms follow. Apparently this reaction is due to a generalized constriction of the pulmonary arteriolar bed that is not limited to the one lobe. This does not explain sudden death which is apparently due to anoxemia unless the emboli occur in both lungs simultaneously.

Disturbance in Function.—Occlusion of the vein may be partial or complete and the results may be temporary or permanent.

Blood must come back by collateral circulation until the thrombus is recanalized or absorbed. It takes many weeks for this to take place, and sometimes it does not occur, in which event the return flow is entirely by collateral veins. At first there is marked edema about the ankle, which may disappear if the collaterals are adequate; if not, a permanent edema remains, because the hydrostatic pressure in the vein is much greater than the osmotic pull of the blood (Chapter 11). Some observers believe that part of the swelling is due to lymphedema (Homans) —that is, that it is the result of obstructed lymphatics as well as veins. Experimentally we can produce edema by ligating a long segment of *vein but not by one ligature. There may be a reflex arterial spasm which* at times is so great that gangrene may occur. Severe degrees of spasm are known as pseudoembolic phlebitis, phlegmasia caerulae dolens, or "blue phlebitis" of Gregoire.

Should the thrombophlebitis persist, a chronic type of inflammation results with acute episodes. Ultimately phlebosclerosis ensues with all the effects of obstruction to the venous return such as chronic edema, cyanosis, pruritis, eczema, ulcer, and varicose veins.

Symptoms.—Early symptoms are obscure; they consist of slight enlargement of the leg, local deep tenderness, increase in tone, and ir-

thrombophlebitis; also in association with nonsuppurative lesions such as erythema nodosum, tuberculosis, and syphilis. (2) Factors *inside the vein*, such as toxins or infections in diphtheria, pneumonia, malaria, typhoid fever, etc., which produce an *inflammation of the intima.* (3) *Changes in the rate of blood flow*, producing stasis, as during long periods of bed rest (especially in old people) or in spinal anesthesia (long period of muscular inactivity), cardiac disease with failure, ischemia from arterial disease. Since venous flow is dependent in a great measure upon muscular action, there is stagnation due to continued immobility. This results in edema. A vasospasm occurs to counteract this loss of blood volume and the reduced blood pressure which accompanies it. This gives rise to an internal pooling of the blood and a shocklike syndrome. The night pains in the legs of individuals with arteriosclerosis are probably due to the above, with a resultant fall in blood pressure and decreased arterial flow. Thrombophlebitis is accompanied by a spasm of the affected vein and its branches peripheral to the lesion and by an arteriolar spasm as well. (4) *Changes in density of the blood*, as seen in starvation, dehydration, and burns (which produce *anhydremia*), polycythemia vera. (5) *Chemical changes in the blood* such as occur in anoxia, perhaps as a result of smoking, and in toxemias of pregnancy and burns; it may be produced by injection into the veins of a hypertonic solution (such as 50 per cent glucose), which irritates the intima (causes 2), destroys the red blood cells, and increases the density of the blood (cause 4). This may occur in long continuous intravenous drips of isotonic solutions, due to the irritation by the needle. It is also seen after intravenous injection of mercurial diuretics, penicillin, and other drugs. (6) Without any known cause a thrombophlebitis may develop. (7) In association with thromboangiitis obliterans by direct extension. (8) As recurrent idiopathic thrombophlebitis (phlebitis migrans). (9) Venospasm from any cause.

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are important in causing thrombophlebitis. Early mobilization is mandatory since normally most of the blood is in the veins. Judiciously used, this one procedure is perhaps the most important single preventive measure. Since phlebothrombosis is most common in the smaller veins of the leg, peroneal, anterior, and posterior tibial, the lower legs must be actively moved. Carefully planned anatomical incisions with meticulous closing permits early ambulation. The surgeon must keep the factors of wound healing in mind. One of these is rest to the part. If early ambulation prevents wound healing, thrombosis may occur at the wound site and give rise to emboli besides other complications such as dehiscence and local infection which also are conducive to thrombophlebitis. Therefore, early ambulation will not be possible in every case, but this should be our goal. If the patient cannot be trusted out of bed because of the condition of the wound, he should be encouraged to take deep breaths, exercise the arms and legs, turn frequently from side to side. The back rest is probably conducive to venous stasis. Since thrombi may form soon after the operation has begun, the anesthetist should be told far enough in advance to discontinue the anesthetic agent so that the patient may be moving soon after he leaves the surgery. Narcotics are used sparingly and immediately after their use; patients are told to move about and walk if possible. Indeed we are really "cruel" in our niggardly use of morphine. Nothing is more conducive to stasis than to keep a patient completely narcotized lying motionless, with slow shallow breathing. (4) Hemoconcentration, dehydration, hypoproteinemia, especially hypoalbuminemia, must be relieved by proper hydration and attention to protein balance. (5) Concentrated solutions are not used—isotonic intravenous therapy is desirable. In chest and other surgery the leg veins are used because of necessity. This is not continued after surgery. The "continuous "drip" has also been abandoned because of its irritation to the veins. *When normal blood flows through normal veins at a normal rate of speed, intravascular clotting does not occur.* (6) Particular attention to the foregoing routine is given obese people, those with varicose veins, and those with arterial disease of the extremities. (7) Prevention of vasospasm on the arterial and venous side may be accomplished by blocking the sympathetics by paravertebral injection of Novocain; also by the use of tetraethylammonium bromide or chloride. The drug is given intramuscularly in the dose of 20 mg. per kilogram. A 10 per cent solution—100 mg. per cubic centimeter is used and the maximal dose ranges from 1 to 1.2 Gm. Priscoline hydrochloride, 25 mg. every six hours, given by mouth, is easier to administer and equally effective. Vasodilation secured as outlined is probably a direct thwart to nature's protective vasoconstriction which increases end pressure and thus lateral pressure. Since most of the blood is in the veins, especially when the muscles in which they lie are immobile, and since on coughing or straining intravenous pressure is further increased

ritability of the calf muscles. Later there are spontaneous pain and pain on forced dorsiflexion of the foot (Homan's sign). Later still an inexplicable rise in pulse and temperature and some pleurisy pain are present. The less dangerous variety of thrombophlebitis begins with chill and an aching sensation down the leg, usually the left leg. Some say phlebitis in the left leg is due to the fact that the left iliac vein is crossed by the right common iliac artery (Homans denies this). There may be swelling of the ankle if thrombosis is extensive or complete. Sometimes there is redness over the femoral vein (inner side of thigh), and usually there is tenderness on palpation. One of the outstanding symptoms of venous thrombosis anywhere is *severe pain* which may be due to distention of the venous wall, arterial spasm, local anoxia, or combinations of these factors. The pain occurs in the leg in the hemorrhoidal veins (thrombosed hemorrhoids), in the lateral sinus in connection with mastoid disease, and especially in mesenteric venous thrombosis. In this latter condition the pain is as severe as in acute pancreatitis. One of the outstanding differential diagnostic features is the presence of blood in the stools. If the physician is on the lookout for phlebothrombosis, he will be less apt to miss it.

Prevention.—Postoperative phlebothrombosis and thrombophlebitis are preventable to a great degree but not entirely so. A glance at the probable causes will reveal the clue to prevention. These facts may be listed as follows: (1) The surgeon must constantly remind himself that veins are injured locally by surgical trauma. As a result of local inflammation and swelling due to this trauma, venous stasis is present distal to the area. This is particularly true in pelvic operations where the crucial veins lie which receive blood from the lower extremities. Once again the aphorism given in Chapter 1 reasserts itself—Handle the tissues with loving kindness and they with their veins will respond in like manner. (2) Septicemias and bacteremias should be controlled as much as possible by antibiotics and chemotherapeutic agents before surgery to avoid inflammation of the intima. Also these same agents may prevent postoperative infections. We must not rely too much on such agents. One of the most conspicuous examples of postoperative infections is that of cystitis following catheterization. This is particularly true in male patients. After such commonplace operations as hernia repair and hemorroidectomy, catheterization was a routine postoperative procedure which was entrusted to orderlies who were supposedly trained to catheterize aseptically and gently. A high incidence of cystitis resulted, with fever, dysuria, and prolonged bed rest. Here the bacteremia and stasis were conducive to thrombophlebitis and actually the complication was common following herniorrhaphy. Now our patients stand up beside the bed to void as soon as they are awake from their anesthetic—catheterization is unnecessary and thrombophlebitis extremely rare. (3) Changes in the rate of blood flow, producing stasis,

ensue. However, new and more competent collaterals quickly form to carry blood back to the heart. The patient must be careful about bruises, injuries, etc. for local immunity is decreased and infections or ulcers may occur. Intermittent external pressure over the entire extremity by elastic bandage should be used three or four times a day. This increases the fluid pressure in the tissue spaces until it is higher than the intravenous pressure, thus preventing further transudation and forcing fluid back into the veins and lymphatics. Ultimately this may cure the patient of the edema (postphlebitic). If the superficial veins are *competent, this method is very effective, for in addition to the foregoing,* adequate collaterals usually form.

2. The use of heparin, as outlined in Chapter 4, subcutaneously in Pitkin's menstruum or Depoheparin and/or Dicumarol and early ambulation. Their use has also been advocated after pulmonary embolism has occurred.

3. Vein ligation with or without thrombectomy. If early thrombectomy should be done—if late and not too difficult, thrombectomy may relieve the patient of many of *the late complications of thrombophlebitis.* Some even advocate bilateral femoral ligation prophylactically. In phlebothrombosis ligation of the superficial femoral does not prevent thrombosis in the deep, and ligation of one common femoral does not prevent thrombosis in the opposite vein; moreover, in iliofemoral thrombophlebitis both iliacs may have to be tied, and this has led to the ligation of the inferior vena cava below the renal veins. This seems to be a safe procedure in competent hands and collateral circulation is established by way of the *vertebrals, azygos, intercostals,* and superior vena cava. The procedure has even been suggested as an aid to the edema of long-standing thrombophlebitis by providing adequate collaterals. We have been opposed to vein ligation as a prophylactic or routine measure even after a single embolus. The dangers of vena caval ligation or bilateral iliac ligation are small but present. This adds another major operation to the patient's illness, with immobilization during and after the procedure—at least during the operation. Minor states of thrombophlebitis *with little tendency to postphlebitic complications* are converted into a true occlusive thrombophlebitis which is apt to be followed by sequelae. Most important is the fact that ligation per se does not guarantee against further thrombosis. In fact, a thrombus may form at the site of the ligature which may propagate. Large rapidly fatal emboli have been successfully removed (pulmonary embolectomy—Trendelenburg operation) in a few cases. This requires quick work with everything in readiness Thoracotomy is done and the clot removed from the pulmonary artery. For those patients who survive long enough for the procedure to be done, recovery is more likely without than with the operation usually.

4. Inactivation of regional *sympathetics* by injection of Novocain, tetraethylammonium bromide, Priscoline hydrochloride, or sympathetic

(Valsalva's experiment), the venous distention may dislodge a thrombus in early phlebothrombosis. With the drop in venous pressure during the next inspiration, the blood and thrombi are sucked and pushed up into the right heart, causing pulmonary embolism. To avoid this some have advocated pressure bandages to the legs before and after surgery. In my *Synopsis of Principles of Surgery*, under Prevention of Thrombophlebitis, I stated: "Perhaps the wisest treatment, once the condition occurs, is to cover the leg with an elastic bandage and permit gentle active (not passive) motion. This, with an anodyne to relieve pain, is all that is necessary." (8) Anticoagulants have been advocated by some—Dicumarol (3-3′-methylbis [4-hydroxycoumarin]) and heparin have been used. We do not consider this necessary as a routine postoperative procedure and the danger of hemorrhage must be considered together with the toxic effects of Dicumarol.

In a study made in 1936 of postoperative deaths in Indiana University Medical Center, for a period of five years, we found that in 5,133 so-called major operations, there were 155 deaths, a general mortality rate of about 3 per cent. Of this group, 53, or about 35 per cent of the deaths, were due to what we termed circulatory causes, an incidence of about 1 per cent. This we divided into cardiac, arterial, venous causes, and hematogenic shock.

Of the 53 circulatory deaths, 18 were due to venous thrombosis and embolism. In 1941, which was four years later, we again assembled our statistics. There were 8,979 major operations studied, and there were 162 deaths, a general mortality rate of 1.8 per cent. Of this group, 68, or 42 per cent of the deaths, were due to circulatory causes, an incidence of .75 per cent. Of the 68, only 10 were due to venous thrombosis and embolism.

Treatment.—As soon as thrombophlebitis is discovered, active treatment is designed to prevent pulmonary embolism and to ameliorate symptoms. The type of treatment depends somewhat on the veins involved: (1) superficial—the saphenous veins and tributaries, the median basilic and cephalic veins and tributaries, (2) muscular and deep veins of the calf, (3) popliteal and femoral veins, (4) iliofemoral veins, (5) axillary and subclavian. Also treatment will vary with the type of thrombophlebitis, depending on its cause and whether it is acute or chronic. In general the treatment which may be used in the acute variety is divided into four types:

1. Massage is strictly prohibited. The application of heat relaxes the venous and arteriolar spasm and hastens involution. After about two weeks the thrombus becomes adherent and is finally recanalized, or the vein is permanently occluded. If the patient also has varicose veins, they should be excised, for they are incompetent and do not really help the blood to return. If all return were interrupted, there would result an enormous swelling, due to edema, and ultimately, even gangrene would

into two main ducts—the right lymphatic duct (which may be double) empties into the right subclavian vein, and the thoracic duct empties into the left internal jugular or subclavian vein. Thus each main lymph channel empties into a large vein and the opening is guarded by a valve. The great veins at the root of the neck have a negative pressure and lymph is actually sucked into them during inspiration. Lymph is also propelled by muscular action and arterial pulsation as well as by external pressure. *The lymphatic system is therefore a closed one.* The lymphatics are almost as numerous as the blood capillaries and probably have a surface available for absorption even greater than the blood capillaries. There are valves in the tubular lymphatics just as in the veins, permitting flow only toward the neck, but no contractile element such as the Rouget cells. However, the endothelial cells are phagocytic. Fascial planes and spaces, mucocutaneous junctions, tendon sheaths, joints, and the pleural and peritoneal cavities are richly supplied with lymph vessels.

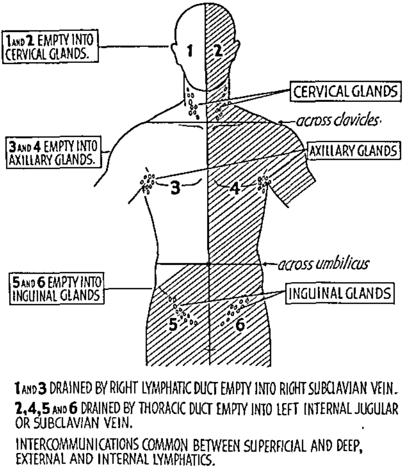

Fig. 188.—External lymphatics. Diagram illustrating roughly the lymph node basins and the areas they drain. The upper transverse line is drawn across the clavicles, the lower through the umbilicus, and the vertical through the midline of the body. Areas 1 and 2 include the head and neck; 3 and 4, the thorax, upper abdomen, and upper extremities; 5 and 6, the lower abdomen and lower extremities.

In general, the lymphatic vascularization of an organ is more abundant as its blood circulation is more active, and lymph vessels are usually more numerous than the blood vessels of the same region or organ. Anastomoses with neighboring lymph vessels are frequent. All lymph vessels except the terminal trunks empty into one or several nodes before they empty into the main ducts. There are exceptions to this occasionally,

ganglionectomy is certainly indicated in the presence of intense and continuous reflex arterial spasm. The first, second, third, and fourth lumbar ganglions are injected with 10 c.c. each of a 1 per cent solution of procaine hydrochloride. In addition, the second and third ganglia are injected with 10 c.c. each of monobromsoligenin (Bronisalizol) solution which inactivates the sympathetics for four to eight days. These procedures do relieve local symptoms, although heat and elevation will usually accomplish the same result. Inactivation of the sympathetics does not prevent extension or embolism; in fact, it may invite it, as shown by the large incidence of thrombophlebitis following sympathetic ganglionectomy.

Summary of Treatment.—We have felt that all facts considered, anticoagulant therapy with early ambulation is the treatment of choice. Rarely ligation may be indicated, but the indications are certainly not clear at present. In those who cannot get out of bed because of the condition of the wound (body casts, etc.), active motion in bed is desirable.

Complications and Sequelae of Thrombophlebitis.—(1) Chronic phlebosclerosis causes edema, superficial varicosities, and pain due to stasis and swelling. Edema may be the cause of ulceration because of interference with circulation and also because edema provides a good medium for bacterial growth. (2) Sudeck's atrophy of bone with muscular atrophy and vasomotor changes. (3) Suppuration in suppurative thrombophlebitis. (4) Gangrene if arterial disease is also present or follows.

Obstruction of large veins by new growth requires their resection. This is feasible and is usually not followed by great and persistent edema although there is usually some. Even portions of the vena cava have been resected below the renals with good results. Small areas of constriction due to fibrosis may be resected and anastomosed. Recently experimental anastomosis has been accomplished between the azygos vein and superior vena cava, azygos vein to atrium, and superior vena cava to atrium. These procedures may be useful in treatment of superior vena caval obstructions.

THE LYMPHATIC SYSTEM

The *lymphatic vessels* originate in the embryo as small buds from the endothelium of the right and left subclavian and iliac veins. From here they develop and finally form vessels over the entire body except in the brain and spinal cord, spleen, bone marrow, catilage, sclera, crystalline lens, and cornea, the epithelial tissues and placenta. There are two sets of peripheral lymphatics. The superficial or *reticular lymphatics* and blindly in the dermis and may be compared to a fine-mesh gauze over the entire body so close that even a hypodermic needle cannot miss them. These empty by communicating vessels into the deep or *tubular lymphatics*, which lie on the deep fascia and usually accompany the veins; in fact, all tissues and organs supplied with blood vessels also have lymph vessels except as previously noted. These in turn join the lymph glands or nodes, which lie along the course of the blood vessels, and are grouped into the cervical, the axillary, and the inguinal basins peripherally and the mesenteric, mediastinal, etc., internally. After leaving the nodes, the lymphatics come together

will be discussed in the chapters dealing with the different systems. Here we should consider general differences. Drinker and Warren state that in the dog the heart and lungs are drained by lymphatics which enter the right lymphatic duct and only the upper part of the left lung supplies lymph to the thoracic duct. Also, in at least half of the animals the right lymphatic duct carries chyle. The right lymphatic duct is not always present in man but when it exists it is very short (12 to 17 mm.) and is formed by the confluence of the right jugular trunk, the right subclavian trunk, and the right bronchomediastinal trunk. These three trunks may empty into the right innominate vein or two of them may unite and one remain separate. They carry lymph from the right side of the head and neck, right upper limb, right side of the trunk, including the upper part of the thoracic wall, right lung and pleura, right half of the heart and pericardium, right side of the diaphragm, and the upper surface of the liver.

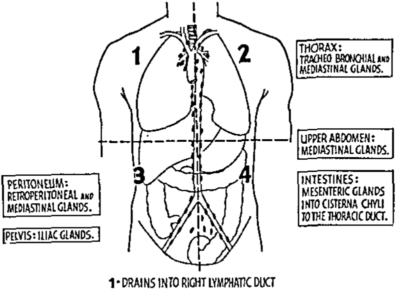

Fig. 189.—Internal lymphatics. Diagram illustrating internal lymph basins. A line is drawn longitudinally through the center of the body and transversely at the level of the attachment of the diaphragm. The superficial glands have connections with the deep basins. The right lymphatic duct gets lymph from the right lung, pericardium, and lower two-thirds of the left lung. The thoracic duct drains the left mediastinum, pericardium, and lung. Chyle is carried almost entirely by the thoracic duct in man but not in lower animals, where as much as 50 per cent is carried by the right lymphatic duct or ducts.

DISEASES OF THE LYMPHATIC VESSELS

Congenital Malformations.—Lymphatics may be absent in different regions. Sometimes it is the nodes that are missing; again lymphatic vessels are either absent or atretic. Such anomalies may produce very few symptoms if collaterals are ample, or there may be transient lymphedemas; more often they are perminent. The transient varieties usually are due to atresia or stenosis or absence of the right lymphatic duct producing chylothorax, the receptaculum chyli producing chylous ascites. Rarely the thoracic duct may be stenosed. The treatment for these types is repeated aspiration as indicated, replacement of lost protein by plasma transfusion, and high protein diet and low fat diet. We have recently had a 9-week-old baby with congenital chylothorax on the

and lymphatics may empty directly into the thoracic duct or the portal system without first passing through a lymph node. Also, efferent vessels of lymph nodes placed at a distance from the base of the neck may empty directly into the veins and the efferent lymph vessels of the thyroid gland may empty directly into the internal jugular vein or into the subclavian vein.

The wall of the thoracic duct differs from the large veins by having a better developed tunica media. The tunica adventitia merges into the surrounding loose connective tissue. It carries the tiny blood vessels which correspond to the vasa vasorum. When injured, the thoracic or right lymphatic duct should be ligated. Collaterals usually form to carry lymph back to the blood stream. Narrow, thin-walled lymphatics are often accompanied by small arteries and veins and capillaries; from these blood vessels encircle the lymph channel.

Physiology

The function of the lymphatics has been mentioned in the discussion of Starling's theory. Since their walls are extremely permeable and there is little or no hydrostatic pressure, they are easily affected by the pressure in the tissue spaces (intercellular spaces). The protein content of lymph is lower than that of blood plasma; therefore, the osmotic pressure is also lower, but the permeability of the lymph vessels enables them to absorb particulate matter (which is often taken up by phagocytic cells) and colloids (proteins). Hudack and McMaster have shown that dyes injected in the skin of the forearm appear in the lymphatics as high as the axilla within eight minutes—faster when gentle intermittent external pressure is applied.

Lymphocytic capillaries differ from blood capillaries in that the former have no gradient or permeation behaving as a semipermeable membrane. In all parts of the body the lymphatics carry away cells and solid substances from the tissues which cannot be absorbed by the blood capillaries. This is especially true of blood proteins which are being lost constantly in varying amounts all over the body except in the renal glomeruli, choroid plexuses, and capillaries of the ciliary body. Thus in all air-breathing animals solid substances and cells get back into the blood stream in spite of blood pressure. In fishes, lymph is forced into veins by contraction of lymph hearts placed on the lymph vessels before their entrance into veins. In frogs and birds the main lymph ducts are paired right and left vessels. If the capillaries lose large amounts of protein due to their increased permeability, in acute inflammations or venous obstructions, the osmotic pressure in the tissues will prevent reabsorption. However, the lymphatics, if open, will carry this protein back to the blood stream, especially if there is movement of the part, massage, or external pressure. Every movement of the body helps in this propulsion, even the pulsation of the arteries.

Lymph vessels in the intestinal villi are known as lacteals and empty finally into the thoracic duct. Their protein content will vary from 2 to 4.5 per cent and their fluid is milky (due to fat) after a meal. The blood capillaries of the liver and portal system are permeable to colloids and here leakage may easily occur if there are obstructions, or inflammations, or variations in protein content. The thoracic duct is therefore busy picking up this lost material through its terminals and returning it to the blood. The peritoneum has many lymph channels which penetrate the diaphragm and empty into the mediastinal glands—thence into the thoracic and right lymphatic ducts. The lymph system, then, is a closed channel whose chief purpose is to return colloid material to the blood, and the lymph is made up of colloids, crystalloids, lymphocytes, and macrophages absorbed from the tissue spaces. Lymph flows slowly (about 4 mm. a second) and only in one direction and that is centripetally; valves at the termination of the main ducts prevent reflux. The amount of lymph flowing through the thoracic duct is from 50 to 120 c.c. per hour.

Great variations from so called normals occur in the lymphatic system. Individual variations occur in different organs and regions. Many of these characteristics

otomy, and esophagectomy when the middle third of the esophagus is involved. Lymphorrhea usually stops with pressure, but chylorrhea does not as a rule. In fact, death may result from chylothorax or chylorrhea due to secondary infection, dehydration, and starvation. The white chyle is easily recognized when the thoracic duct is injured. The duct should be tied at both ends. Collaterals soon form and if the ends are placed in juxtaposition, recanalization may occur. Injuries to the right lymphatic duct are not so serious because lymph is easily carried by other routes and the loss of fluid is not severe.

Obstructions of Lymph Ducts

Obstructions of the lymph ducts may occur from (1) congenital anomalies, (2) trauma, (3) inflammations, (4) new growths, (5) obturations, (6) pressure from without, (7) miscellaneous and unknown causes.

As a result of obstruction to the lymph vessels from any cause there is *lymphangiectasis* or a dilatation of the terminal lymphatics with resultant lymphedema, and as a result of the latter a cellular reaction occurs in the tissues with fibrosis and often ulceration. The term elephantiasis has been used loosely to include any greatly swollen part. Originally it was used to designate the enormous swelling seen after obstruction of large lymph trunks in filariasis. It is not synonymous with lymphedema, since great swellings are often due to plasma edema and are seen in phlegmasia alba dolens and edema of the arm following radical mastectomy.

When the thoracic duct is obstructed within the thorax, a chylothorax may result; in the abdomen, chylous ascites and chyle may appear in the urine (chyluria). It is well known that simple ligation of the thoracic duct does not produce these entities. If the duct is cut and not ligated, chylothorax or chylous ascites results. In neoplasia it is perhaps obstruction and erosion which cause it. If large segments of these ducts are involved, collaterals do not form and chyle is lost. In this respect the thoracic duct behaves as large veins do in the lower and upper extremities (see Chapters 19 and 20).

Congenital Anomalies.—Congenital anomalies have been previously discussed.

Trauma.—Trauma may cause an obstruction by direct division of the ducts or by involvement in subsequent scar formation.

Inflammations.—Inflammations may occur after radical mastectomy, although the vein is also involved.

Acute Lymphangitis.—

Since lymphatics are so permeable, the great danger of a *spreading lymphangitis* is that of spread to adjacent and even distant tissues. An inflammation of the superficial set is known as *reticular lymphangitis* or *erysipelas.* Inflammation of the tubular lymphatics is

right side. Ninety thoracenteses were done over a period of nine weeks, drawing off a total of 12,711 c.c. of chyle. Fluoroscopic studies showed the chyle to be in the right upper posterior portion of the chest near the vertebral gutter and to be encapsulated. The child recovered without further surgery. The more permanent types include simple congenital lymphedema and lymphangiectasis affecting one member of the family and the hereditary type of Milroy's disease. We have recently seen a case of congenital lymphedema of one entire extremity associated with tuberous sclerosis or epiloia. Treatment consists of extensive removal of superficial fascia and suturing the skin to the muscle as described by Homans or using pedicle skin flaps of the thigh and "waltzing" them up onto the abdomen, thereby carrying lymph through these flaps to the lymph channels of the abdominal wall. (See Chapter 6.)

Fig 190.—Cystic hygroma of the neck in 10-month-old infant. Recovery followed surgical excision.

Congenital cysts and lymphangiomas will be considered later in this chapter.

Trauma.—Wounds of larger lymphatic trunks may produce lymphorrhea. This is seen after injuries to the axillary or inguinal basins. Injury to the thoracic duct may follow accidental wounds to the chest—bullet wounds or stab wounds. Sometimes it is injured during surgical procedures such as radical dissections of the neck for carcinoma, phrenic-

etc. Cardiac decompensation with edema leads to dilation of lymph vessels with valvular incompetence, thus increasing the edema already present.

Treatment.—The treatment of various types of lymphedema depends upon their cause. If an obstruction may be removed, the condition may be alleviated. Usually, however, treatment is directed toward reduction of edematous tissue, establishment of collaterals, and protection of the skin against pressure or trauma sores which develop on the slightest provocation.

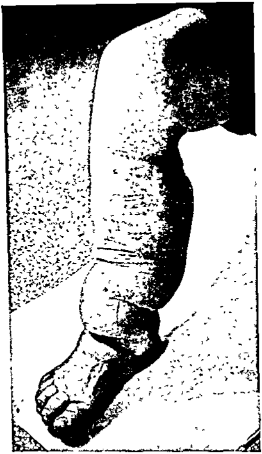

Fig. 191.—Elephantiasis due to chronic lymphedema. The patient was an obese man aged 38 years. The leg had been injured twenty-five years before. A chronic osteomyelitis developed, involving a large part of the tibia. There was extensive cellulitis, with subsequent fibrosis of the lymphatics. Due to the lowered tissue resistance, many superficial infections have developed. The serum protein of the blood was 8.4 gm. per 100 c.c.; that of the edematous fluid, 3.1 Gm. per 100 c.c.

Some of the methods used to develop collaterals have been reviewed in Chapter 6—these consist of rest, elevation, massage, elastic bandage. More radical forms of therapy are as follows: (1) Lymphangioplasty (Handley), which consists of burying long silk sutures in the edematous areas in the hope that new lymph channels would form. In this way a suture would be carried from the edematous areas of the left, for example,

a tubular lymphangitis (see Chapter 5). In three diseases the *tubular lymphatics* may have ulcers along their course: sporotrichosis, tularemia, and tuberculosis. *Acute lymphangitis* described in Chapter 4 as reticular (erysipelas) and tubular may recur periodically as acute inflammations or may become chronic. The tubular type is seen also in anthrax, chancroid (DuCrey's), glanders, syphilis, and even gas bacillus infection.

Chronic lymphangitis may follow an acute attack or it may be associated with venous obstruction as seen in "milk leg" due to thrombophlebitis and arm edema following radical mastectomy or injuries to the axilla. It may be associated with tuberculosis, trichophytosis, sporotrichosis, lymphopathia venereum (Chapter 7) and filariasis (see under Obturation).

New Growths.—When carcinoma cells grow into a lymphatic vessel (as in lymphatic permeation, discussed in Chapter 15), fibrosis occurs about the vessel, due to the irritation it engenders. This is known as *perilymphatic fibrosis* and it ultimately occludes the lymphatics, producing edema. The edematous extremities are easily infected and chronic ulcers form, increasing the edema.

Carcinoma may also obstruct lymphatics by secondary invasion from without.

Obturations.—Obturations may occur as a result of carcinomatous permeation or embolism. Rarer in the United States is the form caused by the *filaria sanguinis hominis* which are embryos living in the blood. The adult worm (Wuchereria [filaria] bancrofti) lives in the lymphatic system. During World War II this disease became common enough to take it out of the category of "tropical elephantiasis" and include it as a possibility in any enlarged part due to lymphedema. If all of the lymphatics of the leg are crippled, great swelling occurs. Local swellings may be due to enlarged lymph nodes, dilated lymph spaces (adenolymphocele), dilated lymph channels (lymphatic varices or lymphangiectasis); hydrocele, chylothorax, chylous ascites, chyluria may occur due to invasion of the genitourinary tract and invasion of the mesentery. Obturation may also occur due to the blood fluke, to Bilharzia hematobia, and to thrombosis of the left subclavian vein where the thoracic duct empties.

Pressure.—Pressure from without on the lymphatics causing obstruction may be due to new growths, enlarged lymph nodes due to tuberculosis, aneurysm, large goiter, particularly intrathoracic.

Idiopathic and Miscellaneous Causes.—Many types of lymphatic obstruction producing lymph stasis and thus lymphedema are idiopathic. In this group is *lymphedema praecox* (Allen and associates) which occurs without known cause in girls between 9 and 25 years of age; also *elephantiasis nostras* in the same group and probably the same entity. Also the various causes may act simultaneously—thus carcinoma by obturation and compression, inflammation by stenosis due to fibrosis and edema,

dium. (5) Cellular or endothelial lymphangioma is a neoplasm arising in the endothelium of lymph vessels. Like the hemangioendotheliomas, it may arise in any organ or tissue, and since blood vessels have small lymphatics about them, a perithelioma arising on perivascular lymphatics has been described. Metastases are rare but local recurrences are frequent.

Treatment.—The treatment varies in the different types. Capillary lymphangioma may be excised or treated with x-ray or carbon dioxide snow. Cavernous types are best excised if feasible. The incidence of postoperative infection is great and recurrence is common. X-ray and radium may be used. Cystic hygroma should be excised. X-ray is of no value and excision should be done before these cysts become secondarily

Fig. 192.—Lymphangioma of the tongue.

infected because this complication may be fatal. Sometimes the endothelial sac is so intimately adherent to the large vessels of the neck that portions of the wall must be left. These areas may be cauterized with phenol and then neutralized with alcohol. The diffuse systemic type is best treated with Kondoleon type operation, but this is often valueless. Postoperative infection is common and amputation may be necessary. Endotheliomas should be excised if possible and then treated with x-rays. If excision is not feasible, x-ray treatment alone causes prompt disappearance of the growth which may, however, soon return.

LYMPH NODES

Lymphatic nodes develop from lymphatic sacs which separate into groups of connected lymphatics, forming the node and filtering the lymph from the area previously drained by the sacs. These areas are usually deep basins such as the deep iliac, jugular,

up to the abdomen. This is not often successful. (2) Kondoleon operation, which consists of bilateral incisions in stages in the leg, extending throughout its length, turning up skin flaps, excising subcutaneous tissue and muscular aponeurosis, and replacing skin. This has not been very successful. The muscle has no lymph and drainage is not restored. (3) Homan's operation is similar to the Kondoleon but is restricted to dissections below the knee. (See Chapter 6.)

Obstructions to the Thoracic Duct

Obstructions to the thoracic duct deserves special mention because of its many causes and its consequences. Many causes have already been mentioned and are included here for completeness. They are (1) obstructions due to outside pressure such as mediastinal tumors, enlarged mediastinal nodes, greatly enlarged heart, aneurysm, intrathoracic goiter, mediastinitis (syphilitic, or tuberculous); (2) involvement of the duct by carcinomatous extension from the lung or nodes, tuberculous processes; (3) obturation by accidental ligature in surgery, filariasis, bilharziasis, neoplastic cells from the abdomen, thrombosis or occlusion of subclavian vein at the duct's entrance. When obstructed, chylothorax, chylous ascites, and even chyluria may ensue.

Lymphangioma

Lymphangiomas, like hemangiomas, may be due to congenital anomalies or may be new growths; a third group is due to lymphatic obstruction, congenital or acquired: (1) The simple *capillary lymphangioma* or lymphatic nevus may be flat or slightly elevated and is recognized by a different color from the surrounding skin, being pink, and by a slight thickening usually following the course of superficial nerves. (2) The *cavernous type* involves the skin and subcutaneous tissue and is composed of dilated and saccular lymph vessels whose endothelium may be greatly thickened; often hemangiomas are associated. Cavernous lymphangioma are seen about the head and neck, the genitals, and mesentery. Frequently they involve the lip or tongue, producing macrocheilia (large lip), macroglossia (large tongue), macromala (large cheeks). When cavernous lymphangioma involves the mesentery, it is known as chylangioma. (3) The cystic type, *cystic hygroma,* is a congenital dilatation of lymph sacs and usually occurs in the neck. We have also removed the growths from the axilla, inguinal region, and retroperitoneal space. They are occasionally seen in the pelvis, thoracic wall, and sacral area. This may be in one or many subdivided compartments. It may be intimately connected with the large vessels and nerves. It transilluminates light and thereby differs from bronchogenic cysts. (4) The diffuse systemic variety involves an entire extremity, producing enormous swelling due to lymphangiectasis; all lymphangiomas are easily infected and this type is particularly prone to be, for lymph is an excellent culture me-

there will be no swelling and an early, perhaps fatal, bacteriemia. The lymph nodes usually stem the tide and then return to normal after the infection is subdued. Occasionally the node breaks down as a result of the infection, and suppuration, with abscess formation, occurs. This requires incision and drainage. There are many *causes for the enlargement of the lymph nodes.* They may be classified as follows:

Infections and Toxemias.—

Acute Lymphadenitis.—Acute lymphadenitis is usually local, with involvement of the particular group of nodes in the area into which the infection drains: the cervical nodes in tonsillitis, the axillary nodes in infections of the hand, the inguinal nodes in infections of the foot, etc. The causative organisms are usually streptococci or staphylococci or both. A section of the node reveals the picture of an acute inflammation, with many polymorphonuclears and macrophages, much vascularity, and swelling. Lymph nodes are a valuable defense mechanism and usually annihilate the invading organism. Sometimes they break down and suppurate, or in long-drawn-out infections they may become fibrotic. Rarely, an infection (streptococcic) may cause no enlargement, in which event bacteriemia results quickly. In acute lymphadenitis the nodes are large and painful (and if near the skin, there is redness and tenderness), with fever and leucocytosis; nodes are also enlarged in tularemia.

Tuberculous Lymphadenitis.—The abscess, instead of being hot and tender, is cold and not painful (cold abscess). The nodes become matted together and undergo liquefaction. Usually the cervical nodes are involved. Children are usually affected and the bovine strain is probably responsible. Formerly extensive excision of these nodes was practiced. This is justifiable if they are the primary and only focus. Since the infection is rarely limited to the nodes, ultraviolet light, x-ray, and sunshine are now used instead of surgery. In most instances the nodes will recede, and recovery is the rule. If a cold abscess forms and breaks through the skin, a chronic sinus results. It will drain until all tuberculous tissue is removed, or until all necrotic tissue is extruded. Histologically, the primary type resembles a nonspecific infection. The adult type shows typical tubercle formation, with caseation.

Syphilitic Lymphadenitis.—The nodes are discrete, usually small, and painless. They do not suppurate or liquefy. With all the other evidences of syphilis, it is not a difficult diagnosis to make. They are seen in primary syphilis in the inguinal region, while in secondary syphilis all of the lymph nodes may be involved. Rarely, tertiary syphilis causes a gummatous formation. The treatment consists of antisyphilitic therapy.

Serum Sickness.—Serum sickness comes on eight or ten days after the giving of horse serum to sensitized patients. It will cause temporary swelling in the nodes, which recedes after forty-eight hours.

etc. Later the peripheral nodes are formed along the course of the lymphatics. The lymph sac is converted into a node by the ingrowth of surrounding mesenchyme, forming bars or partitions. The lymphatic sinuses arise in part as blind anastomosing spaces made from these mesenchymal cells; later these sinuses join with the endothelial-lined afferent and efferent vessels. Some lymphatic sacs remain as such; namely, cysterna chyli and jugular sacs.

The term regional lymph node is used to mean the node or nodes which receive the lymph of the area or organ in that region. This is, to some extent, a misnomer because the nodes may receive lymph from other areas and may not receive all the lymph of the area involved. In general, however, the well-known node basins outlined in the accompanying figures do receive lymph from the areas shown and in that sense are regional nodes.

Lymph nodes do not regenerate well after injury. Instead, they heal by scar tissue formation. As the individual ages, the number of lymph nodes diminishes; at least they diminish in size and become fibrotic, undergoing involutional change. Is this one of the reasons for the slow metastasis of cancer in the aged? Perhaps, but one finds involved nodes in large numbers in advanced cancer at any age.

Hemal nodes may be considered as filters of lymphatic tissue, situated in the course of blood vessels, with function and structures similar to the spleen. They do not occur in man but are found in lower animals, especially ruminants. Their sinuses contain blood and there is no lymph connection.

Lymph node is a better term than lymph gland, although the node has a glandular function. Since other glands exist in the neck particularly, metastasis to glands may be mistaken to mean parotid, submaxillary, or even thyroid gland.

Lymph glands or *nodes* are first seen in the maxillary, iliac, and axillary regions but probably arise from separate islands of tissue. They are small kidney-shaped organs which are found in groups. The lymph vessels enter at the cortex (afferent) and leave the medulla (efferent). When the lymph enters the cortex, it flows freely through a meshwork of reticular tissue which is a *syncytium* of argyrophilic cells. These cells (macrophages) are an important part of the reticuloendothelial system. Whenever bacteria or other foreign bodies are carried into lymph glands, they are engulfed by them. Also, in these meshes are found lymphocytes. The whole mass is penetrated by tortuous lymphatic spaces or sinuses. Their walls are not continuous. The valves of the afferent lymphatics direct the flow toward the node, and the valves of the efferent vessels direct the flow away from the node; that is, the flow is always toward the blood stream. Since the lymph nodes are made up chiefly of lymphocytes and phagocytes, their chief function is dependent on these cells. The former may give rise to fibroblasts, macrophages, polyblasts, and epithelioid cells. In tuberculosis, the latter cells engulf foreign bodies. In addition to the formation of lymphocytes, the lymph nodes act as a filter or sieve, detoxifying, elaborate antibodies (hemolysins and agglutinins), and have bacteriostatic powers. Lymphoid tissue such as occurs in lymph nodes is found in the nasopharynx, intestinal tract, liver, and spleen also.

Infections in Lymph Nodes

Lymph nodes may be termed the "second line of defense" guarding the blood stream. If an infection involves the tubular lymphatics, it will be carried to the lymph glands, causing a tender swelling. This is an excellent defense. If massage or pressure is exerted on an extremity, there will be an increased lymph flow, which will cause a temporary enlargement of the neighboring lymph glands. Lymph node enlargements are due to many causes. The nodes may be fightinng an infection. If the infection is so severe that it goes right through the lymph nodes,

action to this invasion; in others fibrosis occurs. An enlarged node in the vicinity of a carcinoma may not be carcinomatous but inflammatory. This is especially true in late ulcerating carcinoma anywhere in the body, for such carcinomas are usually secondarily infected. This infection occurs earlier in the mouth and in gastrointestinal carcinomas than elsewhere. Large nodes in the neck are difficult to diagnose without biopsy, but this should be withheld until a careful search has been made for a hidden carcinoma of the nasopharynx. Since drainage of lymph into "nodes of the first echelon" may be capricious, occasionally a distant node precedes a proximal one in being invaded. Carcinomatous nodes are usually involved in sequence; therefore, in removing them they should be excised en masse so that lymphatics laden with malignant cells will not be cut across. Some sarcomas metastasize to lymph nodes either directly or indirectly through involvement of adjacent blood vessels.

The treatment of carcinomatous and sarcomatous nodes depends on the extent of the primary growth and the degree of involvement of nodes. In carcinoma of the lower lip, for example, excision of the primary growth and the submental submaxillary nodes is justifiable because these are regional and their early and complete excision may be curative. If, however, distant metastases, which in this instance are rare, are present, this procedure would not be justifiable. X-ray and radium are widely used, the former more than the latter, in addition to surgery or alone.

Malignant Lymphoma.—Malignant lymphoma constitutes a group of *lymphoblastic diseases* of unknown etiology that are usually fatal. A simple classification is as follows: (1) Malignant hyperplasia of lymphoid cells, general or involving a group of lymph nodes; (2) The presence of increased numbers of lymphocytes, usually young or immature lymphocytes in the peripheral blood; (3) Malignant proliferation of lymphoid cells and, in addition, invasion of surrounding tissue; lymphatic leucemia, aleucemic form—factor (1); lymphatic leucemia—factors (1) and (2); lymphosarcoma—factors (1) and (3) lympholeucosarcoma or leucosarcoma (acute lymphatic leucemia)—factors (1), (2), and (3).

The lymphoid cells in the different types look alike and are indistinguishable to most pathologists. The gross appearance of lymph nodes likewise is not characteristic. Hodgkin's disease probably belongs in a class by itself because of its varied behavior but is included here in the lymphoblastomas.

Lymphatic Leucemia.—All lymph glands and lymphoid tissues are enlarged and there is a great increase in the number of lymphocytes: small mononuclears in the chronic and large mononuclears in the acute type. The white blood cells will sometimes reach 150,000 to 200,000 per cubic millimeter. Blood platelets are reduced, causing a tendency to hemorrhage. It is a disease of the bone marrow as well as of the lymph

Lymphogranuloma Inguinale.—Lymphogranuloma inguinale is a disease caused by a filtrable virus (see Chapter 7). The lymph nodes break down, forming draining sinuses. The treatment is the Frei antigen, or excision, penicillin, or streptomycin.

Miscellaneous causes are: yaws, virus diseases, infections, mononucleosis, Ducrey bacillus. Virus infections usually cause a swelling of the lymph nodes and lymphoid tissue in the intestines and elsewhere. This may explain the frequency of appendicitis in colds, influenza, measles, and poliomyelitis. Blood counts are normal or low but rise with appendicitis.

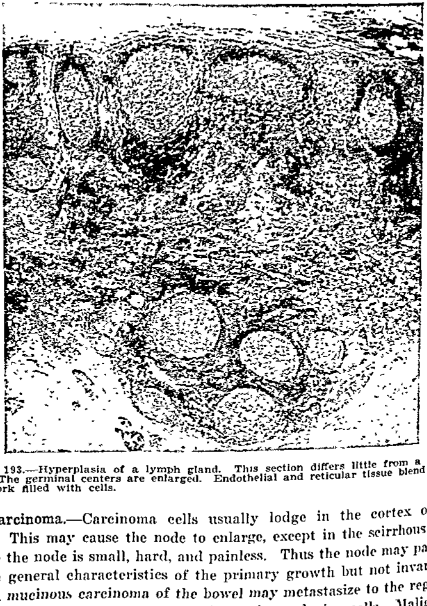

Fig. 193.—Hyperplasia of a lymph gland. This section differs little from a normal node. The germinal centers are enlarged. Endothelial and reticular tissue blend into a meshwork filled with cells.

Carcinoma.—Carcinoma cells usually lodge in the cortex of the node. This may cause the node to enlarge, except in the scirrhous type, where the node is small, hard, and painless. Thus the node may partake of the general characteristics of the primary growth but not invariably so. *A mucinous carcinoma of the bowel may* metastasize to the regional nodes which may or may not contain mucin-producing cells. Malignant cells may grow in the cortex of the node and permeate the deeper sinuses and thus involve other nodes. Some nodes show an inflammatory re-

creased. The treatment is x-ray, which may arrest but does not cure the disease. Nitrogen mustard, methyl bis (2 chloroethyl) amine hydrochloride may help ameliorate symptoms.

Lymphosarcoma.—Lymphosarcoma is a malignancy of the lymph glands. The glands are enlarged, painless, and discrete. X-ray causes a prompt diminution in size and is therefore diagnostic but not curative. The microscopic picture presents a monotonous replacement of the node by malignant mononuclear cells. There is an associated anemia.

Chloroma.—In addition to the conditions which have been outlined, a disease known as chloroma, lying midway between lymphoblastomas and new growths, is occasionally seen. Lymphoid tissue everywhere is involved and has a greenish appearance.

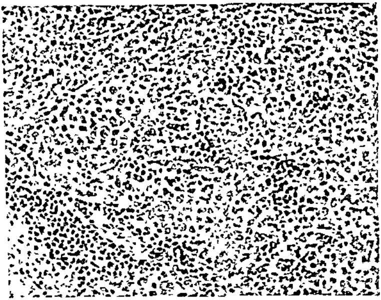

Fig. 195.—Aleucemic reticulocytoma. Lymph gland. showing enlarged reticulo-endothelial cells.

Summary.—Lymph nodes, then, may enlarge physiologically, through simple hypertrophy and hyperplasia, to meet an increasing demand for lymphocytes; or pathologically, from infections, new growths, or causes as yet unknown. A pathological enlargement of the lymph nodes constitutes a *system disease*—that is, a disease apparently limited to the lymph nodes, the bone marrow, and, in the leucemias, to lymphoid tissue. Diagnosis in every case is made by blood counts, sternal puncture for bone marrow study, and biopsy. The bone marrow and lymph nodes are the manufacturing plants and storehouses for cells entering the peripheral blood. If they contain many abnormal or unusual cells, then the peripheral blood will ultimately have them in most cases; therefore, the advisability for bone marrow and lymph node study. Diagnosis is always difficult, especially in children. Although the malignant lympho-

nodes. The histological picture in the nodes is one of hyperplasia of the germinal centers, with masses of lymphocytes scattered everywhere among the fine reticulum. X-ray therapy will help diminish the size of the nodes but will not arrest the disease. Recently folic acid antagonists have been used with some slight improvement. The principal drugs in this group are aminopterin (4-aminopteryol-glutamic acid) and aminoanfol (4-aminopteryol-aspartic acid).

Aleucemic Leucemia.—Aleucemic leucemia is a lymphoblastoma of bone marrow without dissemination. The blood count is low. In taking a sample of the bone marrow, one finds a typical picture of abnormal cells. This may be a forerunner of lymphatic leucemia.

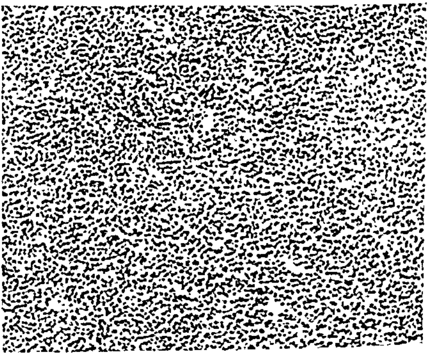

Fig. 194.—Lymphosarcoma. There is a monotonous field of abnormal lymphocytes.

Hodgkin's Disease, Lymphadenoma, or Lymphogranuloma.—The glands may be enlarged over the entire body or may be more pronounced in one group, as in the neck. They are hard and discrete. A relapsing type of fever is often seen (Pel-Ebstein). The microscopic picture of the gland is not always characteristic, but the Dorothy Reed cell (a special type of macrophage) and the increase in eosinophils are said to be characteristic. This picture varies from that of a nonspecific lymphadenitis in the early stage to lymphosarcoma in the late stages. There is itching and dermatitis, with pigmentation. Since in addition to the skin the liver, lungs, kidneys, bones, and central nervous system may be involved, some have classified it as a malignant new growth, Hodgkin's sarcoma, spreading by metastasis. The blood platelets are usually in-

mas are almost invariably fatal, physicians must continue their classification and study with the hope that an ultimate solution of the problem will appear.

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TABLE XV

TUMOR AND TUMORLIKE CONDITIONS OF THE LYMPHOCYTE, THE MYELOCYTE, THE ERYTHROCYTE, AND THE RETICULUM CELL

(Modified from Collander [Lymphatic Tumor Division of American Registry of Pathology, Army Med. Museum]: Am. J. Path., 1934.)

ADULT CELL TYPE	LYMPHOCYTE	MYELOGENOUS		RETICULUM CELL	
		GRANULOCYTES	RED BLOOD CORPUSCLES	RETICULOCYTE MONOCYTE	HODGKIN'S DISEASE
Reactions to stimulation	*"Lymphoma"; lymphocytosis	Leucocytosis	Symptomatic polycythemia	Gaucher's disease; Niemann-Pick disease	
Proliferation of neoplastic type	Leucemic lymphocytoma (lymphatic leucemia): (1) chronic; (2) acute	Leucemic myelocytoma (myeloid leucemia): (1) chronic; (2) acute	(1) Polycythemia vera; (2) leucemic erythrocytoma	Leucemic reticulocytoma (monocytic leucemia)	
Not in peripheral blood	Aleucemic lymphocytoma (aleucemic leucemia) (lymphatic pseudoleucemia): (1) diffuse; (2) nodular	Aleucemic myelocytoma: (1) single; (2) multiple (multiple myeloma)	†Aleucemic erythrocytoma	Aleucemic reticulocytoma (aleucemic reticulosis)	Generalized
Malignant tumors	Lymphosarcoma: (1) without leucemic blood; (2) lymphosarcoma with leucemic blood	Myelosarcoma: (1) taleucemic; (2) leucemic (myelocytic leucosarcoma and myeloid chloroma)	Erythrosarcoma: (1) taleucemic; (2) leucemic	Reticulum cell sarcoma	Sarcomatous

*Applied by some to local hyperplasia due to inflammation.
†Not observed in Registry material.

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Chapter 18

THE NERVOUS SYSTEM

The nervous system is almost entirely ectodermal in origin and its basis is the *neural plate* which folds into a *neural groove* bounded on each side by a *neural fold*. Soon the folds meet forming the *neural tube*. The cranial and spinal ganglia are derived from the neural or ganglionic crest which lies along the line of junction of the neural plate with the general ectoderm. The neural tube does not give rise to the nerve cells and fibers of the olfactory epithelium and certain cranial ganglia that arise in part from spinal epidermal thickenings called *placodes*.

From the neural tube cells come the neuroblasts which give rise to the nerve cells and the spongioblasts which give rise to the ependymal and neuroglia cells (astrocytes) which make up the supporting tissue of the nervous system. Some spongioblasts are migratory and differentiate into oligodengroglia as well as astrocytes. *Microglia* is usually listed as belonging to the neuroglia. These are ameboid phagocytes and probably originate from mesodermal cells and should be called *mesoglia* (Arey).

The supporting cells of the cerebrospinal ganglia at first seem to be a syncytium in which are neuroblasts. The interstitial elements differentiate into cells which invest the ganglion, *capsule cells,* and those which envelop the axons, *sheath* cells.

The neurilemma sheath (Schwann) is composed of cells from two sources; namely, tissue of the early neural crest and the neural tube by way of the ventral roots. At first the sheath cells enclose bundles of nerve fibers; later, as the cells multiply, the bundles are separated and each fiber has its neurilemma.

The *myelin sheath* begins to appear about the fifth month and is derived from the neurilemma or the axis cylinder or both. In the central nervous system there are no distinct sheaths of Schwann but there are scattered sheath cells which are apparently unable to cause regeneration after injury. See Chapter 3.

Vierordt estimated the number of nerve fibers in the spinal nerve trunks at over 800,000 and the number of fibers in the cranial nerves from the third to the twelfth inclusive at 200,000. Arl estimates the number of fibers in the right and left optic nerves of the human adult at about 2,600,000. This gives a total of 3,600,000 fibers without the olfactory nerves. Since many of these nerve fibers branch as they extend peripherally, this number is only a small fraction of the total, just as the large branches of a tree are only a small part of the total number of twigs.

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The *fifth*, or *trigeminal, nerve* is the greatest sensory nerve of the face, having as its three divisions the (1) ophthalmic, (2) maxillary, and (3) mandibular nerves, all of which have their nuclei in the gasserian ganglion. It is of clinical importance chiefly because of the pain that may occur from irritation of this nerve. Such a state is known as *tic douloureux*. The motor part of the fifth nerve is distributed chiefly to the muscles of mastication.

The *sixth*, or *abducens, nerve* supplies the external rectus of the eye and when it is divided or injured the eyeball rotates to the inner side and produces an *internal squint*.

The *seventh*, or *facial, nerve* is the chief motor nerve of the face and supplies the muscles of expression. When it is injured or diseased so that its function is impaired, the muscles on that side of the face will be paralyzed. The paralysis will be complete if the injury is peripheral and partial if the injury is central because of cross innervation. If the patient is asked to smile, his cheek and mouth will be drawn to the opposite side. This condition is known as *Bell's palsy*.

The sensory portion of the seventh nerve is the *nervus intermedius*, the peripheral fibers of which represent parts of the greater superficial petrosal nerve and the chorda tympani branch of the facial; the central fibers form the nervus intermedium. The cells of these fibers lie in the ganglion genicula of the facial nerve. The nervus intermedius contains afferent sensory and vasodilator (parasympathetic) fibers. The taste buds and mucous membrane of the anterior two-thirds of the tongue are innervated by the chorda tympani, and the mucous membrane of the soft palate and posterior part of the nose send impulses by way of the superior petrosal nerve and the sphenopalatine ganglion. Secretory and vasodilator fibers to the lachrymal gland and palate (superior petrosal nerve) and the submaxillary and sublingual glands (chorda tympani) form the efferent components of these nerves.

The *eighth*, or *acoustic, nerve* is the nerve of hearing. Any disease or injury to this nerve will produce an interference with the functions of hearing or of equilibrium (semicircular canals of the middle ear) so that dizziness may be complained of. *Dizziness*, or *vertigo*, denotes loss of equilibrium manifested as a sense of rotation with reference to surrounding objects in space. The vestibular portion of the membranous labyrinth is the end organ responsible for impulses controlling orientation in space or equilibrium. The causes of this distressing symptom include uneven motion (car and sea sickness); cardiac, renal, vascular diseases, pernicious and severe secondary anemia (produce hyperemia and anemia of labyrinth); leucemia and purpura (produce hemorrhage into labyrinth); toxic vertigo caused by alcohol, tobacco, quinine, salicylates; nitrogen embolism (caisson disease, aviator's), Ménièr's symptom complex (allergic); ocular vertigo; lesions of the cerebellum or cerebellopontine angle such as tumors, cysts, abscesses, vascular anomalies which press

THE CRANIAL NERVES

The senses of man are (1) sight—light, form, and color; (2) taste; (3) touch—deformation of the skin, tickle and vibration sense, and the deep sensibility of muscle; (4) temperature—heat and cold; (5) smell; (6) proprioceptive stimuli from the muscles, tendons, and joints, informing the organism of location in space; (7) changes in position in space through the functional activity of the semicircular canals, the utricle, and the saccule; (8) hearing; (9) pain from skin, muscle and blood vessels; (10) visceroceptive stimuli of which persons are usually unconscious but which probably affect vasomotor, respiratory, and cardiac changes reflexly; for example, the inhibition of respiration from distention of the lungs.

The nerves of special senses are twelve in number (called the cranial nerves) and may be listed as follows:

The *first*, or *olfactory, nerve* is the nerve conveying the sense of smell and has its cells in the anterior lobe of the brain. In new growths in this portion of the brain *anosmia* may occur, providing a useful sign to the neurologist in diagnosis.

The *second*, or *optic, nerve* is the nerve of vision. Its importance from a diagnostic standpoint is that in any increase in intracranial pressure of long standing, the venous return and the cerebrospinal fluid circulation are impeded. This results in edema and there will be what is known as a *choked disc*, which may be seen through the ophthalmoscope. The normal disc is the beginning of the optic nerve in the retina (which is really a part of the brain). Normally it is seen as a slight depression. When choked (papilledema), it is more or less elevated. It leads to the diagnosis of brain tumor. Furthermore, if one side or the other of this nerve is interfered with along its path, various fields of vision will become lost. For example, a growth about the pituitary gland would involve the decussation of the nerve. This would produce a *bitemporal hemianopsia*, whereas if the tumor were behind this area on one or the other side, it would produce a *homonomous hemianopsia*. This would immediately fix the growth in one or the other sides of the occipital lobe or somewhere along the nerve path. Quadrantanopsia means loss of vision in about one-fourth of the visual field. This symptom may lead to a more accurate diagnosis of the site of the lesion.

The *third*, or *oculomotor*, nerve has to do with the control of the muscles of the eye (except the external rectus and superior oblique) and of the upper lids; it also constricts the pupil. When divided or diseased, there is a paralysis of most of the eye muscles and a ptosis of the lids, together with a dilatation of the pupil.

The *fourth*, or *trochlear, nerve* controls the superior oblique muscle. It is rarely injured alone and is usually a part of an ophthalmoplegia. When it is affected, the eye deviates upward and slightly inward.

The *fifth*, or *trigeminal, nerve* is the greatest sensory nerve of the face, having as its three divisions the (1) ophthalmic, (2) maxillary, and (3) mandibular nerves, all of which have their nuclei in the gasserian ganglion. It is of clinical importance chiefly because of the pain that may occur from irritation of this nerve. Such a state is known as *tic douloureux*. The motor part of the fifth nerve is distributed chiefly to the muscles of mastication.

The *sixth*, or *abducens, nerve* supplies the external rectus of the eye and when it is divided or injured the eyeball rotates to the inner side and produces an *internal squint*.

The *seventh*, or *facial, nerve* is the chief motor nerve of the face and supplies the muscles of expression. When it is injured or diseased so that its function is impaired, the muscles on that side of the face will be paralyzed. The paralysis will be complete if the injury is peripheral and partial if the injury is central because of cross innervation. If the patient is asked to smile, his cheek and mouth will be drawn to the opposite side. This condition is known as *Bell's palsy*.

The sensory portion of the seventh nerve is the *nervus intermedius*, the peripheral fibers of which represent parts of the greater superficial petrosal nerve and the chorda tympani branch of the facial; the central fibers form the nervus intermedium. The cells of these fibers lie in the ganglion genicula of the facial nerve. The nervus intermedius contains afferent sensory and vasodilator (parasympathetic) fibers. The taste buds and mucous membrane of the anterior two-thirds of the tongue are innervated by the chorda tympani, and the mucous membrane of the soft palate and posterior part of the nose send impulses by way of the superior petrosal nerve and the sphenopalatine ganglion. Secretory and vasodilator fibers to the lachrymal gland and palate (superior petrosal nerve) and the submaxillary and sublingual glands (chorda tympani) form the efferent components of these nerves.

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is made on the part of the divided nerve into which the new fibers have grown (Tinel's sign); also by a short chronaxia and by response to faradic stimulation of muscle.

Factors which influence repair are the same as those which affect other tissues (see Chapter 3). However, some special considerations must be given nerve tissue in regard to time of suture of the divided nerve, methods of suture, infection, length of immobilization, soft tissue defects, nerve grafts.

Time of Suture.—Surgical opinion is divided on the proper time for the suture of a divided nerve. Some surgeons believe that if a wound is seen within eight to ten hours and if it is not the result of a high velocity bullet or a tearing injury, primary suture is indicated. If seen after this time, even if the wound is due to a sharp instrument, three to four weeks should elapse before suturing. Indeed there are those who aver that there is a better prospect of a good recovery after an early secondary than after primary suture. This teaching is contrary to the principles we have enunciated in Chapters 3 and 16. Here we stated that primary approximation of the divided nerve stump is always advisable and that failures are due to the six factors described but especially poor technique, inadequate resection of the damaged nerve ends, excessive tension, and lack of immobilization for a long enough period (three weeks at least). The reasons given for delayed suture are: (1) adequate facilities for immediate repair are not always available; (2) the patient may not be in condition to withstand a time-consuming careful repair; (3) intraneural damage is difficult to estimate at the time of injury, especially when made by high velocity bullets or crushing injuries; (4) mobilization and transplantation of the nerve in badly contused tissue may be followed by infection; (5) the epineurium is thin and friable and lacks the tensile strength to hold sutures; (6) often the wound must be extended in order to mobilize the nerve ends; (7) early delayed suture (say eight to ten days) finds the nerve ends edematous; (8) primary approximation so that the nerves do not retract is wrong because neuromas form as well as scars requiring resection of greater lengths; (9) nerves lying free are covered with fibrin and are swollen, whereas those protected by muscle are not fibrosed. In military surgery it is perhaps best to treat the primary wounds as previously outlined (Chapters 3 and 16) and if possible the nerve should be covered by muscle, and then within three to four weeks after the primary wound has healed solidly the nerve may be approximated. In civilian practice if the wound is early (six to eight hours) primary suture may be done after careful débridement. Late wounds (twelve to twenty-four hours), if due to a sharp instrument, may be treated by primary suture and incomplete closure of the soft tissue wound. Contused wounds after eight hours or incised wounds after twenty-four hours should be left open (late late wounds) and nerves should be repaired six to eight weeks later.

on the acoustic nerves; disseminated sclerosis; aural vertigo (trauma to the ear, basal skull fractures involving the labyrinth, concussions, otosclerosis); infections in and around the labyrinth (labyrinthitis and perilabyrinthitis as in mastoid infections); tumors of the acoustic nerve. The common growth involving this nerve is neurofibroma or neurilemmoma (acoustic neuroma).

The *ninth*, or *glossopharyngeal, nerve* innervates the tongue and pharynx. It has some sensory function (taste) on the posterior portion of the tongue and supplies motor fibers to the stylopharyngeus muscles. Secretory and vasodilator fibers to the parotid gland go by way of the tympanic branch, lesser superficial petrosal nerve, and otic ganglion. The sinus nerve, a branch of the glossopharyngeal, carries the afferent fibers of the carotid sinus reflex arc (Chapter 14). Injury or disease of the nerve interferes with swallowing and sense of taste. Inflammation of the sensory part may produce pain in the pharynx and posterior part of the mouth.

The *tenth*, or *vagus nerve* is the chief nerve of the autonomic (*parasympathetic*) nervous system and has branches to the heart, lungs, intestinal tract, bronchi, and gall bladder. It contains sensory, motor, secretory, and perhaps vasodilator fibers to these organs.

The *eleventh*, or *spinal accessory, nerve* supplies the trapezius muscles and when it is cut or diseased there is a drooping of the shoulder. Formerly this nerve was used as a transplant in the event that the facial nerve had been destroyed. The bulbar part fibers join the vagus in the jugular foramen and are distributed in the pharyngeal and recurrent branches of the vagus and innervate the muscles of the larynx (except cricothyroid), the pharynx, and soft palate (except tensor veli palatini).

The *twelfth*, or *hypoglossal, nerve* is purely motor to the muscles of the tongue. Paralysis of one nerve will cause the *tongue to deviate* to the unparalyzed side since it is literally pulled out by muscles which are unopposed.

PERIPHERAL NERVES

We have already considered the pathological changes that occur in a nerve when it is divided and nature's method of repair (Chapter 3). Needless to say, a peripheral nerve is usually a mixed one and contains not only many sensory fibers, but motor fibers as well. Injury to such nerves produces deficiencies in both functions.

War experience has contributed much to the knowledge of nerve regeneration after injury. Operations performed on severed nerves months after injury have revealed that nerve fibers will find their way into distal segments provided the gap is not too great and foreign bodies do not intervene. Nerve function also returns as evidenced by a return of a tingling sensation along the reinnervated field when pressure

The *phrenic nerve* is the chief nerve of the diaphragm. It comes from the cervical plexus. When it is injured or divided, the diaphragm becomes paralyzed on that side and rises to a point of extreme elevation (expiration). The phrenic is often crushed or divided in the treatment of basal pulmonary tuberculosis and chronic empyema to facilitate obliteration of the cavity; also in congenitally short esophagus, esophageal hiatus hernia (at times), esophagectomy, and certain types of congenital diaphragmatic hernia (see Chapters 8, 19, and 20).

Hiccup, or singultus, is said to be due to an irritation of the phrenic nerve. There is a sudden contraction of the diaphragm and a snapping closure of the glottis, which may be due to a spasm of the adductor muscles of the vocal cords or to the sudden inrush of air (Homans). It is commonly seen after some gastric irritation and is usually transient and trivial. However, it may persist for long periods.

Postoperatively it is seen after abdominal operations or in association with renal insufficiency. In addition to its annoyance, it may delay repair of the wound, interfere with nutrition, and so exhaust the patient as to become alarming. Other conditions in which hiccup may occur are peritonitis, intestinal obstruction, paralytic ileus, diaphragmatic injuries, and encephalitis.

Some type of treatment is known to every layman. Such remedies as snuff to produce sneezing, rebreathing in a paper bag, gulping hot water, sweet spirit of niter, etc., are commonly used. Perhaps the most effective treatment is the administration of 5 to 10 per cent mixtures of CO_2 in oxygen. In a recent accident case (fractures of many ribs, with probable diaphragmatic injury) hiccup developed and could not be controlled by CO_2, morphine, codeine, phenobarbital, or other remedies. The phrenic nerve area on the injured side was infiltrated with 1 per cent procaine solution (with Adrenalin), bringing temporary relief, and after three such injections the hiccups ceased.

The *brachial plexus* is made up of fibers from the fourth, fifth, sixth, seventh, and eighth cervical and the first thoracic nerves. It may be injured in childbirth and, if so, there is paralysis of certain arm muscles and disturbances of sensation.

Sensory disturbances are loss of light touch (epicritic sense), pinprick (protopathic sense), and complete anesthesia (except deep muscle sense, which apparently is carried by other nerves than those supplying the skin). Whenever a sensory nerve is injured, the periphery of the area supplied loses the epicritic sense, and the center of the area, the protopathic sense as well. All zones overlap, as do nerve areas normally.

Motor disturbances are chiefly muscular. The location of motor end plates has been well worked out by physiologists and if the appropriate area is stimulated by the galvanic current (on the make or break) or the faradic current (continuously applied), the muscles can be made to contract.

Methods of Suture.—A conventional method of suturing nerves has been described in Chapter 3. This consists of uniting the connective tissue nerve sheath with fine silk sutures or with tantalum wire. Objections to this method of approximation are based on the following observations: (1) inclusion of nerve fibers in each suture, especially in small nerves; (2) knuckling of fibers when sutures are tied; (3) difficulty in introducing sutures evenly and resultant axial rotation with misdirection of fibers into unmatched "geographical" patterns; (4) adhesions to surrounding tissues. Although methods of "splinting" the nerve by the use of plasma clot, fibrinogen-thrombin, Gelfoam and tantalum foil have been advocated in place of sutures, it seems desirable to hold the nerve ends in opposition by carefully introduced silk, cotton, or wire suture. The plasma clot splint may be used as an additional safeguard. However, a graft of subcutaneous tissue around the suture line may be equally effective to prevent vicious adhesions. If the amount of nerve loss is too great to be approximated without tension, then nerve grafts should be employed. As in other tissues, autogenous grafts give the best results although isogenous and homogenous grafts have yielded good results. Regenerating nerve fibers are preceded by Schwann cells and follow the path of proliferating histiocytes. Since the graft gets its blood supply from surrounding tissue, it is better not to cover the graft with plasma clot or other material. The graft is held in place by carefully placed sutures. Autogenous grafts are difficult to obtain except, for example, where all of the nerves of the arm have been severed except the radial. Here it would be justifiable to use part of the ulnar to repair the median in an attempt to regain sensory and motor function on the thumb and forefinger. Nerves should be immobilized for at least three weeks.

Soft Tissue Defects.—Soft tissue defects are treated in accordance with the principles described in Chapter 16. In the late late wounds, reconstructive procedures, such as excision of scars, or inadequate grafts, or correction of bone defects, may include nerve repair at the same time that full-thickness grafts or other corrective procedures are instituted.

Infection.—Infection is a contraindication to primary nerve suture. However, peripheral nerves have a strong resistance to infection and may heal in the presence of an abscess. The same is true of nerve grafts. The destruction of surrounding muscle, tendon, fat, and fascia by the infection leads to the production of much granulation tissue and scar and may thus prevent proper nerve regeneration.

By knowing the various fields which are supplied by such nerves and the various muscles which such nerves may govern, one is able to diagnose the nerve involved and to repair the same if possible. Later, contractions of a muscle on closing or opening of a circuit conveying a direct current will gradually disappear when the "reaction of degeneration" occurs. A few examples of this may be given as illustrations.

Birth Injuries

Erb-Duchenne (upper arm paralysis) includes the fifth and part of the sixth cervical nerve. This would include the axillary and radial, and therefore the arm hangs (paralysis of the abductors of the shoulder), with extension and pronation of the forearm (paralysis of flexors and supinators of forearm); sensory disturbances are slight. The injury may be caused at birth by pulling the head away from the shoulder, or the shoulder may be forced down; in either case the upper cord is involved.

Klumpke, or lower arm, paralysis involves a part of the eighth cervical and first thoracic nerve. This would include the ulnar (intrinsic *muscles of the hand) and a part of the median (long flexors of median).* Pulling up on the shoulder may produce the injury at birth.

The entire brachial plexus may be injured at birth when undue force is exerted in difficult deliveries. The treatment is, on the whole, unsatisfactory. Attempts at repair have been largely unsuccessful because of extensive scarring and injury. Massage and electrical stimulation together with proper muscle support will permit fibers to regenerate if the neurolemma has not been too badly torn and distorted.

Incised wounds and other injuries of the brachial plexus should be repaired surgically. The results are not as good as on single nerve injuries, and regeneration is slow due to the distance between the plexus and the hand. However, many excellent results have been reported. Rarely the proximal ends of the less important nerves (long thoracic, anterior thoracic) may be sutured to the distal end of more important nerves (suprascapular, musculocutaneous, axillary nerves) where an anastomosis of the cut ends of the plexus is not feasible. Physical therapy and the attempts to move the arm and fingers are helpful.

Industrial Accidents

In industrial accidents the nerves of the arm and leg may be injured. The position of the nerve, the muscles involved, and the sensory field supplied give the surgeon an accurate diagnosis. For example, division of the *radial nerve* gives rise to *wrist drop* because this nerve supplies most of the extensor muscles of the wrist and fingers. If the injury is low, small sensory fields over the back of the thumb and the forefinger will also become impaired in function. If injured in the upper arm and just above the wrist, it differs from the lower arm in *producing more sensory involvement in* the two former because the dorsal cutaneous comes off high and in the lower forearm fibers from the musculocutaneous join it. Injury to the posterior interosseous branch does not produce wrist drop or sensory disturbances. Dorsiflexion is preserved by the extensor carpi longus. Paralysis of the extensor digitorum communis renders extension of the proximal phalanges impossible, but the distal phalanges retain their movement (interossei and lumbricales).

Four to seven days after division of a nerve there is no response to the faradic current, and after ten days, a sluggish response to the galvanic. This loss of response to faradic and sluggish response to galvanic stimulation is known as the *reaction of degeneration*. If it persists, muscle atrophy and fibrosis occur, but recovery is possible. If there is a *complete reaction of degeneration* (no response at all to galvanic stimulation), recovery is usually not possible. In addition to sensory and motor disturbances, the part becomes cold and blue, indicating sympathetic nerve disturbance.

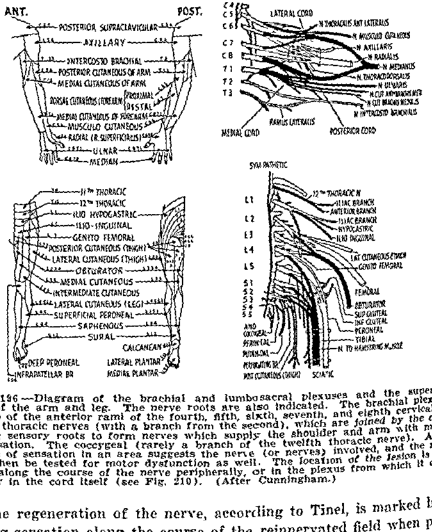

Fig. 196.—Diagram of the brachial and lumbosacral plexuses and the superficial nerves of the arm and leg. The nerve roots are also indicated. The brachial plexus is made up of the anterior rami of the fourth, fifth, sixth, seventh, and eighth cervical and the first thoracic nerves (with a branch from the second), which are joined by the corresponding sensory roots to form nerves which supply the shoulder and arm with motion and sensation. The coccygeal (rarely a branch of the twelfth thoracic nerve). A disturbance of sensation in an area suggests the nerve (or nerves) involved, and the nerve should then be tested for motor dysfunction as well. The location of the lesion is then sought, along the course of the nerve peripherally, or in the plexus from which it originates, or in the cord itself (see Fig. 210). (After Cunningham.)

The regeneration of the nerve, according to Tinel, is marked by a *tingling sensation along the course of the* reinnervated field when pressure is made on the regenerated part of the nerve (that is, peripheral to the part sutured or anastomosed). *The motor part* requires five to seven months or longer before any tonicity is seen in the muscles. Then *voluntary motion slowly returns.* In addition to massage, heat, electrical stimulation, and splinting (to prevent contractures by opposing muscles), *the patient* must try to use his muscles to force stimuli into the regenerated axis cylinders(?).

(pinprick), then laterally to half of third toe and the lateral part of the lower leg. The *tibial nerve* is comparable to the median and ulnar nerves (plantar flexors) and is seldom injured.

Inflammations

In addition to the preceding traumatic considerations, there may be many other causes of nerve disorder which may produce an inflammation of the nerve or an irritation. Such disorders have been called *neuritis* (inflammation of nerve) in the former and *neuralgia* (painful nerve) in the latter event.

A brief grouping of such causes is suggested in the following outline (Homans):

Kinds of Peripheral Neuritis and Neuralgia

1. Injury to peripheral nerves, as in sepsis and fibrosis
   a. Tic douloureux
   b. Neurofibrositis (amputation neuroma)
2. Disease involving nerve trunks
   Septic processes; pressure (abnormalities of the spinal column)
   Multiple neuritis (alcohol, lead, arsenic)
   Tumors (as neurofibromatosis, neurilemmoma)
   Causalgia and ascending neuritis
3. Lesions of posterior roots or posterior root ganglia (herpes)
4. Psychalgias (coccygodynia)

Another *classification into general and local types* is as follows (Cobb and Coggeshal):

1. Generalized polyneuritis
   a. Virus diseases (such as poliomyelitis, herpes, smallpox, epidemic encephalitis, rabies)
   b. Bacterial diseases (such as pneumonia, diphtheria, typhoid, chorea)
   c. Metabolic or deficiency diseases (pellagra, beriberi, sprue, etc.)
   d. Chemical poisoning such as arsenic or lead
2. Localized neuritis
   a. Infections (diphtheria, tetanus, streptococcus, leprosy)
   b. Mechanical causes (pressure, tumor, edema, fibrosis, trauma or local asphyxia, as in Volkmann's contracture)

One of the most common errors of the laity and even of physicians is to call any pain a neuritis. It is true that the pain is a neuralgia, which is another way of saying "pain in a nerve." This is meaningless from a diagnostic point of view. For example, "neuritis" of the arm is commonly a subdeltoid bursitis; neuritis of the leg, sacroiliac disease, sometimes a protruding nucleus pulposus, rarely a spinal cord tumor.

It will be seen, then, from this discussion that pain (sensory) or paralysis (motor) means nerve involvement. It must be decided whether or not the nerve is really affected (neuritis) or is stimulated by disease in its path (neuralgia). Then by a careful study of symptoms and signs,

There is paralysis of extensors of the thumb and the long abductor of the thumb, preventing extension of the thumb and its abduction in the plane of the palm. Thus the thumb reposes in a position of slight flexion, being immediately ventral to the index finger. The posterior interosseous branch may be repaired with a good chance of regeneration.

The *median nerve* supplies the flexors of the wrist except the flexor carpi ulnaris and fingers, the pronators of the forearm, and the opponens and abductor pollicis muscles of the thumb. When the median nerve is injured, the thumb cannot be rolled over on the palm or make the letter "o" with the little finger, nor can it be abducted at right angles to the plane of the palm. The median nerve supplies the sensory area on the palm, from the middle of the ring finger radialward to the thumb, and the area on the back of the second, third, and fourth fingers over their distal portions. These symptoms are characteristic and occur when the median is injured in the region of the elbow. Few symptoms are present when the nerve is injured in the wrist. This is due to the fact that there are no branches in the upper arm, but there are communications with the ulnar in the proximal forearm and in the palm through its cutaneous branches.

The *ulnar nerve*, which is frequently injured, controls the intricate actions of the fingers so that after injury of this nerve the thumb may not be adducted (adductor pollicis) to the side of the hand, and the fingers—particularly the fourth (ring) and fifth (little finger)—may not be extended at the interphalangeal joints nor flexed at the metacarpophalangeal joints (claw hand). The fingers cannot be separated and brought together (interossei). The sensory area supplied by the ulnar is the ulnar one-half of the fourth finger and the anterior part of the fifth finger and extends posteriorly over about the same area. The ulnar lies close to the median and brachial artery in the arm. There are no branches until the forearm. Here it supplies the flexor carpi ulnaris and medial half of the flexor digitorum profundus. The two terminal branches are a superficial, which is purely cutaneous, and a deep, which is purely muscular, supplying the flexor brevis and abductor digiti quinti, opponens digiti quinti, and branches to the interossei, third, and fourth lumbricales, adductor policis, and deep part of flexor policis. It communicates with the median and radial.

If the *common peroneal nerve* in the leg is injured, a situation comparable to wrist drop (from radial nerve injury in the arm) will be seen. However, here it will be *foot drop*. Injury to this nerve is apt to occur when casts are used in the lower leg about the knee, or when operations are done on the fibula, for the nerve winds around the neck of the fibula. Injury to the common peroneal will produce disturbed sensation over an area on the dorsum of the foot, extending as a triangle, with the base over the lateral half of the big toe and medial half of the second toe

ones which are the seat of neurofibrositis, resection of the neuroma, neurectomy, reamputation at higher levels fail to produce a cure.

Experimental evidence is against the opinion that pain impulses traverse the sympathetic ganglion. They probably follow mixed nerves to enter the spinal cord by the posterior roots. However, resection of the posterior roots frequently fails to give relief. The best prophylaxis is, first, an amputation if possible which will permit weight bearing on the stump (Gritti-Stokes; Symes) rather than around the circumference by a boot; second, as little handling of nerves as possible; third, division of the nerve with a sharp scalpel without previous crushing or injection and without subsequent injection of alcohol; and, fourth, division at a high level so that axis cylinders will regenerate into the muscle far above the site of weight-bearing, granulation tissue, and subsequent scarring.

The symptoms and signs include (1) the pain which may be local or along the course of the nerve or the spinal segment; (2) trophic changes; (3) vasomotor disturbances; (4) pain (if present before operation) projected to the same area in the phantom; (5) sensations—warmth, burning, throbbing, piercing, cramping, or cutting.

Treatment is variable and, like the causalgia states, is often ineffective, due to strong psychologic factors. Any local irritation or tumor should be removed; in addition, vasomotor disturbances are benefited by local infiltration with procaine (1 per cent) of the paravertebral sympathetic nerves, and if this is effective but not lasting, sympathetic ganglionectomy is indicated. Where amputation has been done for vascular disease, tetraethylammonium bromide or Priscoline may be useful if sympathetic ganglionectomy is contraindicated, because of the poor physical condition of the patient.

In the more intractable cases anterolateral chordotomy may be helpful. As a last resort cerebral tractotomy may be necessary. But even then the "phantom pain" may persist in the amputated extremity. Therefore, psychotherapy is extremely helpful in all of these patients.

Group 2. Disease Involving Nerve Trunks.—

Causalgia has been discussed in Chapter 6 under Indirect Injury Due to Circulatory Disorders because of the associated vasomotor phenomena. Weir Mitchell first described this syndrome and ascribed its origin to a partial or incomplete injury of a major nerve trunk. The causalgia-like state referred to in Chapter 6 may be due to relatively minor injuries, or indeed the origin may be obscure or entirely unknown. The cutaneous hyperalgesia, burning, rasping pain, and local increase in blood flow with edema to the part involved is a classical picture. Usually the median or sciatic nerves are involved. Almost all forms of treatment have been tried, including direct surgical attack on the injured nerve (neurolysis), drugs, physiotherapy, fever therapy, periarterial sympathectomy, cervico-

the nerve or nerves affected must be found and finally the cause or causes for the condition must, if possible, be discovered. Then treatment will be effective.

However in spite of the most painstaking examination, this may be difficult. This is due to the fact that chronic irritation of a sensory nerve pathway may involve peripheral, spinal, and cortical levels. This will be more apparent if the diagram of a cross section of the spinal cord is consulted. Sensory nerves may be irritated by injury or inflammation or new growth as follows: (1) peripherally in the skin, (2) along the sensory root distal to the dosal root ganglion, (3) in the dorsal root ganglion, (4) proximal to it, (5) in the dorsal horn cells, or (6) the whole afferent neuron may be involved. Similarly the other compartments of the reflex arc may be involved by disease but not producing pain: (1) connector neuron by cord tumor, syringomyelia, etc.; (2) anterior horn cells by anterior poliomyelitis, and (3) the motor nerve trunk anywhere along its course as indicated by local or systemic factors. Furthermore, stimulation anywhere along the course of a sensory nerve may give rise to symptoms and signs locally in the skin, later over the course of the nerve, then a wide zone involving the dorsal cord, and finally the sensory cortex. Thus an amputation neuroma, phantom limb, causalgia, and psychalgia become closely related entities. Moreover, as a result of connector or efferent neuron stimulation, the motor effects may produce pain, or as a result of immobility due to pain secondary changes occur which in themselves are painful.

Thus an outline on neuralgia will be helpful if the foregoing facts are borne in mind and if, in addition, the possibilities are considered, beginning with the periphery where most causes are found and working centrally. A few special types of neuralgia need further consideration.

Group 1. Injury to Peripheral Nerves.—

Neurofibrositis is usually referred to as an *amputation neuroma*, yet the lesion is not a true neuroma but a bundle of axis cylinders, and what is more important, the most painful states do not present a tumor at all. In this group belong *"phantom limb"* with little or severe pain in the amputated extremity. The cause of these pains is not clear and may be due to local irritation of bundles of axis cylinders or a projection from sensory areas of the cerebral cortex. Some have ascribed the condition to psychogenic causes and have branded the patient as psychoneurotic. This is probably not true, although the phantom sensation may be a projection arising from the postcentral sensory association areas in the cerebral cortex.

No doubt the origin is in small neuromas in the stump. It is inconceivable that an operation of any kind can be accomplished without end bulbs or neuromas forming. These may be very small but any stimulus, physical or emotional, may excite them. However, except in the large

ones which are the seat of neurofibrositis, resection of the neuroma, neurectomy, reamputation at higher levels fail to produce a cure.

Experimental evidence is against the opinion that pain impulses traverse the sympathetic ganglion. They probably follow mixed nerves to enter the spinal cord by the posterior roots. However, resection of the posterior roots frequently fails to give relief. The best prophylaxis is, first, an amputation if possible which will permit weight bearing on the stump (Gritti-Stokes; Symes) rather than around the circumference by a boot; second, as little handling of nerves as possible; third, division of the nerve with a sharp scalpel without previous crushing or injection and without subsequent injection of alcohol; and, fourth, division at a high level so that axis cylinders will regenerate into the muscle far above the site of weight-bearing, granulation tissue, and subsequent scarring.

The symptoms and signs include (1) the pain which may be local or along the course of the nerve or the spinal segment; (2) trophic changes; (3) vasomotor disturbances; (4) pain (if present before operation) projected to the same area in the phantom; (5) sensations—warmth, burning, throbbing, piercing, cramping, or cutting.

Treatment is variable and, like the causalgia states, is often ineffective, due to strong psychologic factors. Any local irritation or tumor should be removed; in addition, vasomotor disturbances are benefited by local infiltration with procaine (1 per cent) of the paravertebral sympathetic nerves, and if this is effective but not lasting, sympathetic ganglionectomy is indicated. Where amputation has been done for vascular disease, tetraethylammonium bromide or Priscoline may be useful if sympathetic ganglionectomy is contraindicated, because of the poor physical condition of the patient.

In the more intractable cases anterolateral chordotomy may be helpful. As a last resort cerebral tractotomy may be necessary. But even then the "phantom pain" may persist in the amputated extremity. Therefore, psychotherapy is extremely helpful in all of these patients.

Group 2. Disease Involving Nerve Trunks.—

Causalgia has been discussed in Chapter 6 under Indirect Injury Due to Circulatory Disorders because of the associated vasomotor phenomena. Weir Mitchell first described this syndrome and ascribed its origin to a partial or incomplete injury of a major nerve trunk. The causalgia-like state referred to in Chapter 6 may be due to relatively minor injuries, or indeed the origin may be obscure or entirely unknown. The cutaneous hyperalgesia, burning, rasping pain, and local increase in blood flow with edema to the part involved is a classical picture. Usually the median or sciatic nerves are involved. Almost all forms of treatment have been tried, including direct surgical attack on the injured nerve (neurolysis), drugs, physiotherapy, fever therapy, periarterial sympathectomy, cervico-

dorsal and lumbosacral sympathectomy, and psychotherapy. Of all forms of treatment, sympathectomy and psychotherapy give the best and most lasting results.

Scalenus anticus syndrome. Normally the lowest cord of the brachial plexus passes behind the scalenus anticus muscle and over the first rib. The subclavian artery comes out of the thorax behind the muscle and emerges over the first rib in the angle formed by the scalenus anticus and the first rib. If a cervical rib is present, the nerves and artery are forced to make a more acute bend behind the muscle and over this rib, exposing both to an irritation which may give rise to symptoms as follows: pain over the shoulder, down the arm along the course of the

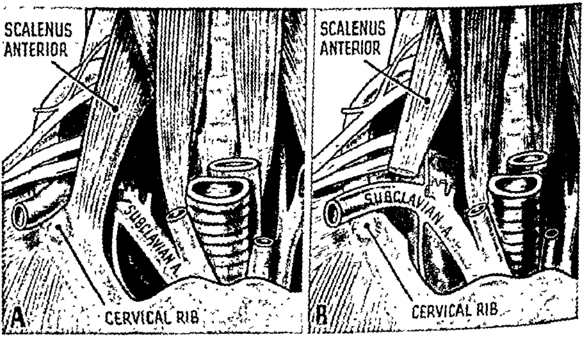

Fig. 197.—Scalenus anticus syndrome. *A*, Diagram illustrating the possible cause of arm pain and vasomotor phenomena. *B*, Division of the anterior scalene muscle and its effect upon this pressure

median and ulnar nerve. If the patient turns his head toward the affected side and raises the elbow, the pain is relieved, and the pain increases if the elbow is lowered. Sometimes vasomotor phenomena appear such as coldness with sweating and bluish discoloration. If much pressure is present on the subclavian, the pulse will be feeble and the blood pressure on the affected side will be lower. If the patient takes a deep breath, elevates his chin, and turns it toward the affected side, pulsations may be obliterated in the subclavian, brachial, and radial. Sometimes feebleness of pulsation is due to atheroma at the site of pressure on the subclavian. This must be remembered during operation, as a "blow out" may occur. Gangrene of the fingers has been reported, and in this way this syndrome resembles Raynaud's disease. Although

the gangrene may be due to spasm or atheroma with thrombosis, a dislodged thrombus, producing embolism, may also be a cause.

Similar symptoms may be present without a cervical rib due to spasm of the scalenus anticus or in congenital malformations of the first rib (rudimentray structure terminating in a synostosis or pseudoarthrosis with the second rib, or free in a free end in the soft tissues with or without a fibrosis band attached to the manubrium).

The syndrome must also be differentiated from cervical arthritis, carcinoma of the lung (Pancoast or superior sulcus carcinoma), metastatic carcinoma of the nodes at the thorax apex, herniation of lower cervical discs, tumors of peripheral nerves, and, very rarely, thromboangitis.

Diagnosis includes careful examination, x-ray studies, and injection of the scalenus muscle with procaine which should give relief if due to spasm.

Treatment in mild cases consists of injection of the muscle with procaine, 1 per cent and exercise of the involved shoulder to strengthen the trapezius and other muscles which elevate the shoulder. In more severe cases treatment includes sectioning of the scalenus anticus tendon at its attachment to the first rib, also any fibers of the scalenus medius which seem tense; resection of the cervical rib or abnormal first thoracic rib must be done to relieve pressure in some cases.

Septic processes and *pressure* involving nerve trunks and producing nerve pain include sinusitis (glossopharyngeal neuralgia), protrusion of one or more intervertebral discs, hypertrophy of ligamenta flava, fractures of the vertebra, spondylitis, radiculitis, traumatic spondylitis, spondylolisthesis, Pott's disease, posttraumatic spondylitis (Kümmel's disease).

Tumors of *peripheral nerves* include neurofibroma and neurilemmoma. The latter is also known as perineural fibroblastoma or schwannoma and is closely related to the carcinoid tumors of the small intestine and appendix which arise in nerve tissue which are related to argentaffin or chromaffin cells. The neurilemma is a membrane made of Schwann's cells and a constricted portion (nodes of Ranvier). The neurilemma as a whole is not connective tissue but is a membrane all its own and is ectodermal in origin. The tumors do behave as connective tissue neoplasms as well as carcinomas. The peripheral types are usually benign. Sometimes they show areas of fatty and cystic degeneration. We removed a cystic perineural fibroblastoma from the axilla of a 40-year-old woman. Our clinical diagnosis was cystic lymphangioma. Neurofibroma does not often occur singly but is usually disseminated, as in von Recklinghausen's disease (see Chapter 16). Ganglioneuromas are usually found in the retroperitoneal or posterior mediastinal spaces. Neuproepitheliomas are rare but highly malignant and require amputation of the extremity if they are present in a limb.

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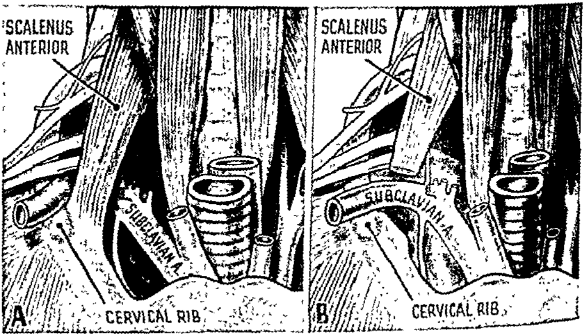

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vitamin B; local neuralgia due to chronic bursitis is only relieved when the irritated bursa is treated by x-ray or removal. Postherpetic neuritis may be helped by physiological salt injections within the roots and in addition by thiamine chloride (vitamin B_1) orally; the sciatic pain produced by a protruding intervertebral disc is relieved by removal of the disc.

THE AUTONOMIC NERVOUS SYSTEM

Sympathetic and Parasympathetic Systems

The nervous system of the body may be said to be in two distinct departments: that which governs voluntary actions and that which is self-governing or controls involuntary actions. The former, as we have seen, is known as the central nervous system and the latter has been called the autonomic nervous system. It is easy to understand why the body must have such a mechanism. The heart works automatically, as do the lungs, intestines, bladder, and glands of internal secretion. However, either system affects the other.

The central nervous system may be said to create the environment (that is, specific action), whereas the autonomic nervous system makes it possible for an individual to become adapted to his environment (more general action). Man is a delicate, and yet a very stable, animal. He is sensitive to sudden changes in temperature, yet his blood temperature stays the same whether he be at the North Pole or at the Equator. If he exercises, more sugar is used and more lactic acid is formed. To offset this, glycogen is taken from the liver and lactic acid is oxidized to carbon dioxide, which is volatile and is given off. To facilitate this, blood pressure, heart rate, and respiration are increased. Thus man maintains his stability (homeostasis, as Cannon has termed it).

The difference between a frog (a cold-blooded animal), who is the victim of its environment, and man (who is a warm-blooded animal) is at least in a great measure due to the control of the autonomic nervous system. Such functions as the stability of the body temperature, the rate of respiration, the successful control of the pH and osmotic index of the blood, the activity of the glands of internal secretion, the mobilization of leucocytes and antibodies, immunities and sensitizations, water balance, vascular adjustments, metabolism of fats and sugars are all partially governed by, and in turn affect, this mechanism.

Anatomically, the autonomic (or vegetative) nervous system is composed of two distinct parts: the sympathetic and the parasympathetic systems.

The *sympathetic* system is found in a series of ganglia lying on either side of the spinal column in the thoracic and lumbar regions. These ganglia are little, white, bean-shaped or flat bodies that are joined to the central nervous system by two sets of fibers: the *white rami communicantes* or *preganglionic* fibers, which run from the anterior horn cells

Group 3. Lesions of Posterior Roots or Posterior Root Ganglia.—Lesions of posterior roots or posterior root ganglia include herpes zoster (shingles). This disease is caused by a virus in all probability and may be contagious. Its relationship to chicken pox has been noted. The severe pain which follows the course of the nerves involved precedes the blisters which appear later, and the pain may remain after cutaneous manifestations have disappeared (postherpetic neuralgia). The important fact to remember is that the pain often mimics visceral disease (gall bladder, pleurisy, appendix, etc.) Treatment is unsatisfactory but pain may be relieved by injection of the nerve roots with procaine solution in physiological saline.

Intercostal pain is important because of its effects on respiration (see Chapter 19). Stimulation of the central end of any intercostal nerve causes a reflex inhibition of respiration and a concomitant fall in blood pressure. The lower intercostal nerves (7 to 12) elicit a greater response than do the upper. Also, stimulation of sensory or intercostal fibers in the diaphragm causes reflex contraction of the abdominal musculature through a reflex connection with other lower intercostal nerves. These observations explain the abdominal and thoracic symptoms in intercostal neuralgia from any cause.

Group 4. Psychalgias.—Psychalgias include many different varieties of neuralgia. However, the term is often loosely used to cover unexplained causes of pain. In this group coccygodynia is often listed, yet occasionally a painful coccyx may be due to a glomus tumor over the coccyx or a bursitis of the sacrococcygeal bursa. The treatment will therefore depend on the cause, and certainly removal of the coccyx rarely produces a cure unless in the removal a glomus tumor or chronically inflamed bursa is also removed. Undoubtedly psychotherapy helps.

Treatment of Neuritis.—Obviously the treatment depends on the cause. Types of treatment may be listed under the following heads:

1. General (treatment of the infection, the deficiency, or the chemical cause)
2. Local
   a. Removal of the pressure, tumor, or fibrosis
   b. Injection of nerve with procaine (for diagnosis), or alcohol (temporary relief), or salt solution (epineural injection) to allay inflammation and perhaps lift the nerve off of its bed.
   c. Excision of the nerve (unmyelinated portion for permanent relief)
   d. Excision of the nerve cells (in those of the semilunar ganglion for tic douloureux
   e. Chordotomy for inoperable carcinoma

To give some examples of treatment, general polyneuritis due to vitamin deficiency may be relieved by supplying an adequate intake of

vitamin B; local neuralgia due to chronic bursitis is only relieved when the irritated bursa is treated by x-ray or removal. Postherpetic neuritis may be helped by physiological salt injections within the roots and in addition by thiamine chloride (vitamin B_1) orally; the sciatic pain produced by a protruding intervertebral disc is relieved by removal of the disc.

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of the spinal cord to the ganglion, and the *gray rami communicantes* or *postganglionic* fibers, which run from the ganglion to the motor nerve. The preganglionic fibers may end in the ganglion, or go up or down the ganglionic chain, or go straight through the ganglion, so that an impulse has a more or less mass effect rather than a specific, local one. Furthermore, the sympathetic nervous system has outlying ganglia, such as the celiac and inferior mesenteric, whose pre- and postganglionic fibers make up the splanchnic nerves, which govern the action of the gastrointestinal

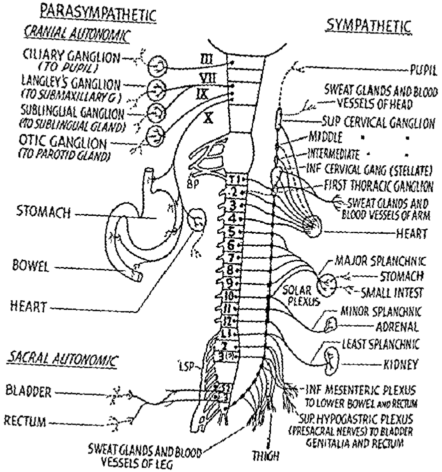

Fig. 198.—Diagram of the autonomic nervous system, showing the sympathetic and parasympathetic systems. BP, brachial plexus; LSP, lumbosacral plexus. (After W. Langdon Brown and Homans.)

tract. And lastly, the sympathetics are intimately related to the adrenal gland, the medulla of which is derived from nerve tissue, so that stimulation of sympathetic nerves may excite the production of adrenaline, which creates a synergistic effect.

Although painful states may be relieved by dividing autonomic nerves, the amelioration is due to a division of true sensory neurons traveling with the autonomic fibers or to a relaxation of the organ as a result of a division of efferent sympathetic or parasympathetic fibers. No *afferent* autonomics have been described.

Impulses are transmitted from the viscera by afferent fibers which pass through the various plexuses and reach the central nervous system through the pelvic, lumbar, splanchnics (greater, lesser, and least splanchnic) and vagus nerves. The afferent fibers of the vagus have their cells in the ganglion jugulare and ganglion nodosum and their central processes in the dorsal nucleus of the vagus. From here connections are made with efferent parasympathetic pathways to complete the reflex arc. The afferent fibers of the pelvic nerve have their cell bodies in the posterior root ganglia of the second, third, and fourth sacral. The afferent fibers of the sympathetic division have their cells in the posterior spinal nerve root ganglia from the first thoracic to the third lumbar. None arise from sympathetic ganglia. They reach the sympathetic trunk by way of the white rami communicantes and are distributed to the viscera along with the corresponding efferent fibers, although afferent fibers are not interrupted in any of the sympathetic ganglia. Some enter the spinal nerves by way of the gray rami for distribution to the limbs.

The *parasympathetic* system originates in the cranial and in the sacral region. The preganglionic fibers are long, the postganglionic fibers short, arising in the glands or muscles they innervate (as the plexus of Auerbach and Meissner) and in the intestinal tract (plexus myentericus and submucosus). The parasympathetic system is partially antagonistic to the sympathetic, and it has been said that whereas the sympathetic nervous system is the "spending" system, the parasympathetic system is the "saving" or "storing" system. When we consider their respective actions, this statement will be more apparent.

The most important nerve of the parasympathetic system is the *vagus*. It has branches to the heart, lungs, and gastrointestinal tract. The sacral parasympathetics control the bladder, colon, rectum, and genital organs. Unlike those of the sympathetic system, the postganglionic fibers lie in the organ itself.

Listed here are a few of the differences between the two systems. It may be said in general that the sympathetics and parasympathetics may be antagonistic to each other but are not necessarily so.

SYMPATHETIC	PARASYMPATHETIC
Vasoconstrictors Sweating	No opposing fibers
Gooseflesh	
Accelerate the heart	Inhibit the heart
Dilate the pupil *and widen palpebral* fissure	Constrict pupil *and narrow palpebral* fissure
Inhibit peristalsis of small and large intestine	Increase peristalsis of small and large intestine
Inhibit antral movements and usually inhibitory to pyloric sphincter	Increase stomach movements and usually excitatory to pyloric sphincter
Diminish secretion	Increase secretion
Relax the bladder and rectum and constrict the sphincters	Contract bladder and rectum and relax sphincters

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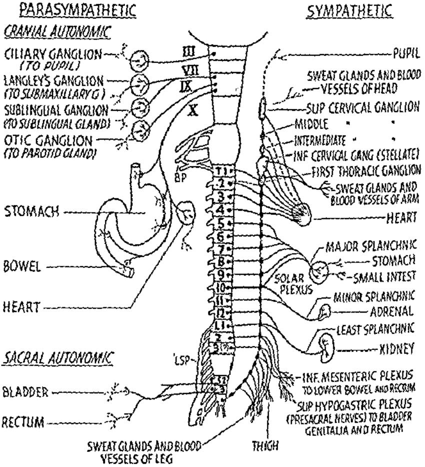

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It is thought that there are centers in the brain (around the third ventricle and lateral to the infundibulum) which control the entire sympathetic nervous system. These centers are under reflex and psychic control.

The *parasympathetic* or *energy-storing* system helps stabilize overactivities of the sympathetics. *Cardioinhibitor nerves* slow the heart. Other nerves stimulate the salivary and digestive glands to activity and promote peristalsis. In this way the parasympathetic system helps digest food; it also aids in excretion (to allow more food to be digested). The sacral parasympathetics empty the rectum and relax the anus and cause contraction of the bladder (detrusor muscle) and relaxation of the sphincter.

Perhaps the autonomics act through chemical substances, *sympathin* and *parasympathin*, which are formed between the nerve ending and the cell. Sympathin possesses the properties of adrenaline (adrenergic); *parasympathin, those of acetylcholine* (cholinergic).

The Action of Drugs Upon the Autonomic Nervous System

Adrenaline has the same effect as stimulation of the *sympathetics*. Sweating is an exception. Denervated effector organs are sensitized to the action of adrenaline. Vasoconstriction occurs everywhere except in the coronaries, the vessels in the intestines, and perhaps skeletal muscles. Pulmonary vessels are unaffected, but in large doses there is vasocontriction and dilation of bronchioles.

Pilocarpine causes *parasympathetic* effects by acting directly upon *the effector cell. These effects are contraction of pupil, cardiac inhibition*, contraction of smooth muscle is bronchioles and alimentary tract, secretion from salivary, gastric, bronchial, and sweat glands.

Muscarine acts like pilocarpine in most of its effects. In addition, it causes vasodilatation. The action is directly on the effector cell.

Choline and its ester, *acetylcholine*, cause *parasympathetic* effects by acting directly on the effector cell. These effects are cardiac inhibition, contraction of smooth muscle of alimentary canal and bladder wall, secretion of saliva, tears, and sweat, dilation of arterioles and fall in blood pressure. Blood and tissue fluids contain an enzyme, cholinesterase, which inactivates acetylcholine. Physostigmine inhibits the action of cholinesterase; therefore, when given with acetylcholine, the latter's action is greatly intensified.

Physostigmine or *eserine* causes *parasympathetic* effects by inhibiting the action of cholinesterase and so permitting the cholinester liberated at the nerve endings to exert its full effects.

Atropine neutralizes parasympathetic effects by acting directly on the effector cell, thus preventing the action if not the liberation of acetylcholine. It is antagonistic to pilocarpine and muscarine. Thus there is an increase in pulse rate, dilation of pupils, decrease in secretion of saliva

The sympathetic and parasympathetic systems in the thorax act differently from the way they act in the rest of the body. For example, the sympathetics carry the cardioaccelerator nerves, and the vagus (parasympathetic) carries the cardioinhibitory nerves. Whereas over the entire body the sympathetics cause constriction of blood vessels, in the heart the sympathetics cause vasodilatation and parasympathetics cause vasoconstriction. The pulmonary circulation is probably not under vasomotor control. In experimental animals (dog) vasoconstrictor as well as vasodilator fibers are found in the sympathetics and the vagus. The prevailing opinion is that vasoconstrictors are predominantly in the sympathetics as in the periphery of the body. However, it is unlikely that effects of exercise, for example, would cause increased activity without provision for adequate blood supply (see Chapter 19).

The sympathetics cause dilatation of the finer bronchi, and the parasympathetics, constriction. It is well known that division of the sympathetics often relieves bronchiolar spasm in asthma. This may not be as paradoxical as it seems, for improvement may be due to the vasoconstriction which ensues, due to the free action of adrenaline on the sympathectomized bronchioles.

Pilocarpine, histamine, and foreign proteins cause bronchiolar spasm. Animals who have died of anaphylactic shock show a constriction of the bronchioles. Air is trapped in the alveoli and the lungs fail to collapse even when the thorax is opened. Adrenaline, ephedrine, and atropine relax bronchi and, in addition, adrenaline causes vasoconstriction of bronchial vessels.

It is important to know that even after the sympathetic and parasympathetic nerves to an organ have been cut that organ seems to have enough inherent nerve control to take care of its autonomic functions. However, if all of the autonomics were permanently and completely interrupted, man would lose his freedom and become as much the victim of his environment as his amphibian ancestors.

Some have attempted to group certain individuals who complain of various functional derangements into classes called *sympathicotonia* (overaction of sympathetics) and *vagotonia* (overaction of parasympathetics). These symptom groups are vague and ill defined.

The *sympathetic* or *energy-spending* system is activated transiently during anger according to Cannon. Arteries are constricted, there is sweating, hair stands on end, "goose flesh" appears, pupils dilate, palpebral fissures widen, and secretions of gastrointestinal glands are inhibited. Through action on the smooth fibers in the spleen, contraction occurs, affording more cells to the circulation (see Chapter 13). The adrenal medulla (chromaffin cells) pours out adrenaline which reinforces sympathetic activities and calls glucose from the liver for use in the active muscles. Cardioaccelerators are stimulated, making the heart beat faster.

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Pilocarpine causes *parasympathetic* effects by acting directly upon *the effector cell. These effects are contraction of pupil, cardiac inhibition,* contraction of smooth muscle is bronchioles and alimentary tract, secretion from salivary, gastric, bronchial, and sweat glands.

Muscarine acts like pilocarpine in most of its effects. In addition, it causes vasodilatation. The action is directly on the effector cell.

Choline and its ester, *acetylcholine*, cause *parasympathetic* effects by acting directly on the effector cell. These effects are cardiac inhibition, contraction of smooth muscle of alimentary canal and bladder wall, secretion of saliva, tears, and sweat, dilation of arterioles and fall in blood pressure. Blood and tissue fluids contain an enzyme, cholinesterase, which inactivates acetylcholine. Physostigmine inhibits the action of cholinesterase; therefore, when given with acetylcholine, the latter's action is greatly intensified.

Physostigmine or *eserine* causes *parasympathetic* effects by inhibiting the action of cholinesterase and so permitting the cholinester liberated at the nerve endings to exert its full effects.

Atropine neutralizes parasympathetic effects by acting directly on the effector cell, thus preventing the action if not the liberation of acetylcholine. It is antagonistic to pilocarpine and muscarine. Thus there is an increase in pulse rate, dilation of pupils, decrease in secretion of saliva

and gastric juice and sweat as well as nasal and bronchial gland secretion It lowers the tone of bronchial and gastrointestinal muscles.

Nicotine is useful in locating ganglion cells which it paralyzes or the synapse between the cell and the preganglionic fiber.

When the body needs *general action*, the *hormones* are liberated rather than the nerve impulses themselves.

Clinical Application

The most direct *application* of this knowledge seems to be in the treatment of peripheral vascular diseases such as Raynaud's, thromboangiitis obliterans (chapter 6), vasospasm following injury to arteries, operations on blood vessels (see Chapter 17), causalgia (Chapter 6), and "phantom limb." This is especially true in Raynaud's disease, where the removal of the sympathetic ganglia will convert a cold, moist, bluish, painful extremity into a warm, dry, painless member.

White believes that if complete sympathetic denervation is accomplished, the vessels are left to the mercy of adrenaline, to which they become hypersensitive.

Furthermore, operations on the sympathetics have been used in the treatment of malignant hypertension (splanchnicotomy), painful states such as angina pectoris (cervical sympathetic neurectomy), pericoronary neurectomy in coronary disease, painful menstruation (presacral neurectomy), and likewise in diseases such as megacolon or Hirschsprung's disease (resection of the inferior mesenteric and superior hypogastric-presacral), and also diseases of the bladder.

A great many minor states that develop as a result of imbalance or overaction of the autonomics may ultimately be relieved by surgery. This field of endeavor is still in its infancy and its application may well be extended to include such intractable states as the chronic arthritides, asthma, irritable colon, and nonspecific ileitis (with constriction).

One is struck with the thought that the granulomatous and fibrotic masses found in certain nonspecific bowel lesions may be initiated in spasm. There is no proof of this theory except the relationship of scleroderma, Raynaud's disease, cardiospasm with achalasia of the esophagus, and regional enteritis and colitis. Some observers maintain that the permanent effects of splanchnicotomy and other operations for malignant hypertension have been found to be no better than after any nonspecific operation.

Horner's Syndrome.—Injury to the cervical sympathetics or invasion by neoplasia may cause a cessation of sympathetic impulses producing Horner's syndrome; namely, contraction of the pupil, enophthalmus, pseudoptosis (that is the upper lid can be raised voluntarily), absence of flushing and sweating in the corresponding side of the face and ear.

Stimulation of the cervical sympathetics cause dilatation of the pupil and flushing and sweating of the face and ear.

Carotid Sinus and Carotid Body.—The physiology of the carotid sinus has been discussed in Chapter 14. The sinus and aortic nerves are important in controlling blood pressure and maintaining the circulation of the brain. Changes from recumbent to the sitting position, loss of fluid or blood volume, etc., result in vasoconstriction and cardioacceleration, elevating blood pressure. Head-down position, vomiting, cough, hydremic plethora, and fear result in vasodilation and cardioinhibition and a fall in blood pressure. The bradycardia is probably by way of the sinus nerve as the vagus is unresponsive to mechanical stimulation. Sometimes paroxysmal tachycardia may be stopped by pressure above the sinus (increasing intraluminal pressure at the bifurcation of the carotid), or nausea and vomiting may be induced with ipecac having the same effect. Only about 30 per cent of normal persons have a carotid sinus which is sensitive to external pressure. In those who are sensitive, a *carotid sinus syndrome* or *vasovagal syncope* (Lewis) may occur. This manifests itself by attacks of dizziness and fainting and sometimes convulsive seizures which result from overactivity of the sinus reflex. During an attack there is a bradycardia and fall in blood pressure. There may be extrasystoles, delay in the auriculoventricular conduction, or complete heart block (Stokes-Adams). Sometimes denervation of the sinus is necessary to ameliorate the symptoms.

The *carotid body* is thought to be derived from the embryonic ganglion cells of the sympathetics. Other theories are that it comes from the epithelium of the pharynx, endothelium, or adventitia of the carotid artery. The function of the carotid body (and also the aortic bodies) is due to the presence within them of chemoreceptors which respond to chemical changes in the blood. These respond to oxygen tension, whereas the respiratory center responds to carbon dioxide tension. They also respond to H ion concentration. Both bodies may be removed without any apparent symptoms. Sometimes carotid body tumors arise. These are usually benign but may be malignant. The diagnosis is based on the palpation of a tumor at the bifurcation and rarely systemic disturbances such as malaise, headaches, and depression. The treatment consists of removal. However, it may be necessary to ligate the common and internal carotids. If a Horner's syndrome or recurrent laryngeal nerve paralysis exists, the growth is probably malignant and has invaded surrounding structures. The mortality (30 per cent) and the morbidity (80 per cent) following surgery is more often due to the ligations rather than to the extirpation of the growth. Therefore, gradual carotid compression is used as a preliminary measure.

Essential Hypertension.—Although the exact cause of essential hypertension is not known, a very logical explanation is based on the work of Goldblatt. He showed by his experiments that any interference

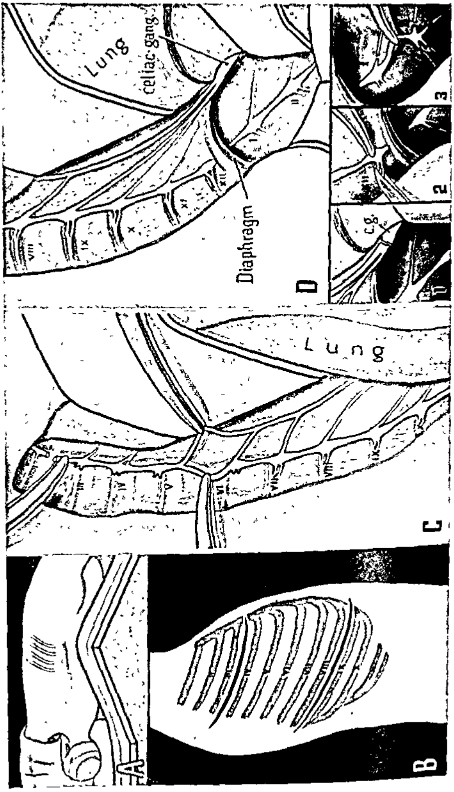
Lung
celiac gang.
Diaphragm
D
c.g.
1
2
3
Lung
C
B
A

Fig. 199.—Operative technique of thoracolumbar sympathectomy. (Modified from Hinton and Lord.) *A.* Position of the patient on the table. *B.* Incision in the third interspace to get the inferior cervical, first, second and third thoracic ganglia. Incision in the bed of the ninth or tenth rib to get the lower thoracic ganglia, the first and second lumbar, and the greater and lesser and least splanchnic nerves. Many surgeons use an extrapleural type of operation. We have preferred to make the operation a transpleural. *C.* The chest is opened through the eighth interspace, the ribs are spread apart, and the nerves are dissected out after the mediastinal pleura has been opened directly over the nerve bed. *D.* The lower part of the operation requires opening of the diaphragm, and with the wide exposure gained by this maneuver the entire chain may be easily removed, the adrenal may be inspected, and biopsy of the kidney taken. *1*, *2*, and *3* show method of grasping each ganglion and severing of the ganglion from its junction with the intercostal nerve The chain is grasped with a long curved remostat and is carefully dissected from each intercostal artery and vein. Then the communicating rami are divided several millimeters from the ganglia. The greater splanchnic nerve usually has its origin from thoracic ganglia *6*, *7*, *8*, and *9*. It pierces the crus of the diaphragm and joins the anterior end of the celiac ganglion. In its course in the thorax the splanchnic ganglion is usually formed. The lesser splanchnic nerve arises from the gangliated trunk opposite the ninth and tenth ganglia and ends in the celiac plexus. The lowest splanchnic nerve arises from the twelfth thoracic ganglion or from the lesser splanchnic nerve and then pierces the diaphragm and ends in the renal plexus. In this way it is possible to remove the entire thoracic ganglia, the upper two lumbars, and the greater, lesser, and lowest splanchnic nerves. The greater splanchnic nerve is divided at its junction with the celiac ganglia.

with the hemodynamic state of the kidney produces a continuous elevation of blood pressure without evidence of impaired renal excretion. This is now known as the renal humoral theory since many observers believe that the elevated blood pressure is due to an excessive amount of "renin" which reacts with "preangiotonin" to produce "angiotonin," the pressor substance.

Based on this hypothesis and the experimental evidence that electrical stimulation of the splanchnics causes hypertension, presumably producing a renal ischemia, the operation of splanchnicectomy has been used. This then is comparable to sympathectomy in Raynaud's disease for in both there is, for unknown reasons, overactivity of the sympathetics. The operation does produce an increase in renal blood flow and many cures have been produced by the operation before irreversible kidney damage has occurred. The splanchnics (greater, lesser, and least) may be interrupted below the diaphragm (Adson and Craig), above the diaphragm (Peet), and both above and below the diaphragm (Smithwick); there may be almost complete denervation, including the celiac ganglion (Grimson).

Improvement in techniques has made extensive sympathetic ganglionectomy safe. The transthoracic approach is easiest and best. An incision is made in the third interspace posterolaterally, and the upper dorsal ganglia from the third or fourth down are removed. Then another is made in the eighth interspace, and the lower dorsal and upper lumbar ganglia together with the splanchnics may be excised. This is facilitated by incising the diaphragm. Hinton and Lord have done the entire procedure through the bed of the resected ninth or tenth rib. The parietal pleura is reflected from the chest wall, exposing the diaphrgam which is divided, and the retroperitoneal space entered. The chain and the splanchnics are dissected from each intercostal artery and the communicating rami are divided several millimeters from each ganglion. The twelfth ganglion is usually located in the substance of the diaphragm or just above it. The chain is attenuated between the twelfth thoracic and first lumbar ganglia. Following this extensive procedure, orthostatic hypotension is so great that an inflatable "corset" must be used to prevent collapse for a short period. The results are encouraging although permanent cures are not too common and orthostatic hypotension may be a serious handicap.

New Growths.—New growths of the sympathetic ganglia are known as ganglioneuromas. Most of these occur along the route of cervico-thoracico-lumbar chain, some are formed in the suprarenal medulla, and others arise in widely separated ganglia. Most ganglioneuromas are fully differentiated, benign, and do not metastasize; some are partially differentiated and do metastasize, and a few are mixed or pure sympathicoblastoma which are highly malignant and metastasize rapidly.

THE SCALP AND SKULL

The scalp is composed of the following five layers and covers the cranium, which is the bony covering of the brain.

1. The *skin.*
2. The *subcutaneous tissue* is a firm fibrous layer binding the skin to the layer below by strong fibrous septa. In this layer are the blood vessels and nerves.
3. The *aponeurotic layer,* which is in reality the aponeurosis of the occipital frontalis muscle, is loosely applied to the underlying subaponeurotic layer.
4. The *subaponeurotic layer* is made up of loose areolar tissue.
5. The *pericranium* is really the outer covering or periosteum of the skull.

It will be noticed that the first three layers are united as one, but the aponeurotic layer may be easily separated from the cranium. The aponeurotic layer, also known as the galea, is attached to the skull posteriorly (external occipital protuberance), laterally (temporal muscle), and anteriorly (superciliary ridges). This is important, because collections of fluid or pus beneath this layer gravitate to the points of attachment. Furthermore, should a wound extend down to the galea, very little gaping would occur. If, however, the galea were divided transversely, there would not only be gaping, but also avulsion if the force were sufficiently strong. The Indians knew this when they practiced scalping. The blood supply of the scalp is from below upward; consequently, if there is any attachment left, the flap remains viable. This is the reason in brain surgery for making scalp flaps with the lower portion attached.

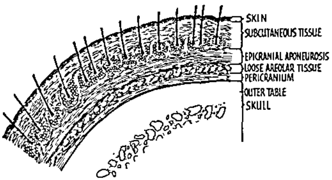

Fig. 200.—The scalp is composed of the following layers: skin; subcutaneous tissue, which contains blood vessels and nerves; aponeurotic layer (*galea aponeurotica, epicranial aponeurosis*), which is the aponeurosis of the occipitofrontalis muscle; the loose subaponeurotic layer; and the pericranium. The outer three layers are adherent to each other.

Injuries of the scalp demand careful inspection for possible skull fracture with brain injury. The hair must be shaved and all foreign bodies carefully removed by frequent washings. Bleeding is usually profuse because the blood vessels in the subcutaneous layer cannot retract and contract as in looser tissues; therefore, hemostasis is accomplished by loose suture.

Infections of the scalp are either localized (carbuncle, furuncle) or diffuse (cellulitis). The treatment is the same as elsewhere, except one must remember that there is a connection between the scalp and the intracranial sinuses through the diploic and emissary veins. Should collections of pus or serum occur beneath the galea, drainage is dependent; that is, at points of attachment (q.v.)..

Tumors and cysts of the scalp are common, especially sebaceous cysts, or wens. These are due to occluded sebaceous ducts and may grow to the size of a hen's egg or larger. They are easily excised. Perhaps the most common tumor is a hemangioma. X-ray films should be made to determine whether these vascular tumors have any intracranial connections (sinus pericranii).

Caput succedaneum is an edema of the scalp of the newborn. It occurs over the part which presented and is probably due to pressure against the rigid external os. *Cephalhematoma* is also seen in the newborn and is due to hemorrhage beneath the pericranium. This swelling is usually limited to one bone, for the pericranium is attached at suture lines. The treatment is entirely conservative for the former and also the latter, unless the hemorrhage remains unabsorbed; in this event, aspiration is done.

The *cranium* is the bony cage within which lies the brain. It is made of membranous bones which heal only by fibrous tissue (because callus swellings would press upon brain tissue). These bones have an outer table covered by pericranium and an inner table lined with the dura mater. Between the tables is the diploe, a loose space containing many communicating veins. The diploic veins carry blood in both directions and emissary veins transport blood from the sinuses to the scalp veins. The sutures of the skull lie *anteriorly* between the frontal and parietal bones, *sagitally* between the parietals, *posteriorly* between the parietals and occipitals, and *laterally* between the parietals and temporals. These sutures are defective at birth—in front and back (anterior and posterior fontanel) and laterally. This arrangement of the six fontanels and the suture lines allows for "molding" during birth and prevents excessive intracranial pressure. The anterior fontanel closes at about 2 years of age; the others, shortly after birth. The obstetrician is able to diagnose fetal position by feeling the fontanels. The suture lines unite at about 40 years of age or thereafter. If because of malnutrition, or disease, or unknown causes, the suture lines and fontanels close prematurely or remain open unusually long, certain *anomalies* present themselves and give various sizes and shapes to the skull. Among these are *microcephaly* (small skull), *oxycephaly* (pointed skull), the large skull of hydrocephalus, etc. Certain bony landmarks of the skull should be remembered for they are frequently used in anatomic descriptions: the bregma, glabella, nasion, inion, and pterion.

Infections of the skull occur as in other bones (see Chapter 21) but are more dangerous because of the possibility of extension into the brain or its coverings. *Osteitis* is a nonspecific infection of bone usually following infection of the scalp and must be relieved by drainage. Large areas of necrotic bone may slough. The process is extremely chronic. The x-ray is invaluable in the diagnosis and shows the amount and progress of the lesion. Tuberculosis is rare but syphilis is common, especially of the con-

genital type (see Chapter 14) and is treated by antisyphilitic remedies. A destructive syphilitic lesion is known as *craniotabes.*

Metabolic and nutritional disorders produce changes in the shape and density of the bone: rickets produces a square or sugar-loaf head, acromegaly, a small head with prominent brows and jaw, while xanthomatosis (Schüller-Christian disease) multiple myeloma, and Ewing's endothelioma produce a moth-eaten appearance of the cranium.

Tumors of the cranium are not uncommon. *Meningiomas* arise from the dura but frequently involve the bone, whereas *osteomas* may arise directly from bone. Both types tend to be slow growing and benign and may be completely removed, relieving brain pressure.

Fig. 201.—Osteoma of the skull.

Injuries of the meninges are described later in the chapter. However, subdural hematoma (pachymeningitis interna hemorrhagica) which results from an injury may produce spasms or convulsions and therefore may require surgical intervention.

Infections of the meninges are known as *meningitis* and if the dura alone is involved (from injury or extension from the skull) it is known as *pachymeningitis.* This must be rare, for the leptomeninges are almost always involved also. Meningitis may be epidemic in type (that is, that caused by the meningococcus). Syphilis, tuberculosis, and toxins produced by a number of organisms may affect the meninges. The treatment is conservative with perhaps occasional spinal drainage and the use of sulfadiazine and penicillin. In tuberculosis the prognosis was

formerly always fatal. Streptomycin offers a much better outlook (see Chapter 8). In other types the outlook is still better, but in none is it real good.

THE MENINGES AND BRAIN

The brain is covered by three membranes known as *meninges*. The outermost is attached to the inner table of the skull and is known as the *dura mater*. It also spreads to form the falx and tentorium. The *arachnoid* covers the brain snugly but does not dip into its convolutions as does the third layer, the *pia mater*, which carries the blood vessels. In some places (as where the arachnoid passes over a gyrus) the pia and arachnoid are connected by dense trabeculae and they appear as a single membrane. The expanded portions are the cisternae which communicate with each other. The larger branches of the arteries and veins of the brain traverse the subarachnoid space. Their walls are directly connected with the subarachnoid trabeculae and are bathed by subarachnoid fluid. Some of the arteries are closely attached to the pia mater. The blood vessels that penetrate the pia are surrounded by perivascular spaces but are not connected with lymph vessels as was formerly thought. They are connected with the subarachnoid space. The finer twigs ramify in the pia before entering the substance of the brain and as they enter they carry sheaths from the pia. The pia and arachnoid together are also known as the *leptomeninges*. The space between the two is known as the subarachnoid space through which flows the cerebrospinal fluid (normally 60 c.c.). This fluid is of the utmost importance, for it forms a layer in the ventricles and subarachnoid space which relieves pressure on the brain within its rigid vault. In coughing, sneezing, injuries, inflammation, and new growths, this is the great equalizer of pressure—until its limits are reached. This fluid is formed chiefly in the *choroid plexuses* which are located in the lateral ventricles and third and fourth ventricles (although some is formed by the cells lining the subarachnoid space). The four places in the brain occupied by these plexuses retains its embryonic character as thin epithelium—lamina epithelialis. The pia mater which covers this epithelium is very vascular and is closely joined to the lamina epithelialis, forming the tela choroidea. The tela choroidea is irregular and folded, protruding into the ventricle so that a great free surface full of blood vessels is exposed to the ventricles. The epithelium is different from the ependymal cells which line the ventricles. It is cuboidal and is composed of one layer. These cells store dyes as do the fixed macrophages in the perivascular connective tissue. The leptomeninges have no such function. The subarachnoid space is carried outward for a short distance on the nerves in connection with their arachnoidal sheaths and communicates with the lymph channels of the nerves. This is especially true in the oldfactory, optic, and acoustic nerves. Some observers believe that there is a communication between the subarachnoid space and the lymph vessels of the nasal mucous membranes. Dandy believed that cerebrospinal fluid is absorbed from the entire subarachnoid space in to the capillaries of the pia arachnoid and denied the existence of arachnoidal villi or pacchionian granulations. His experiments show that when the cerebral hemispheres are separated from the longitudinal and transverse sinuses on both sides, leaving only the rolandic vein attached (no pacchionian granulations), absorption of cerebrospinal fluid was unimpaired.

The vessel walls and the pia must be traversed for fluid to get out (Drinker and Fields). This double membrane may account for the high degree of impermeability of the choroid plexus not only to much of the blood proteins, but to other more diffusable substances as well. Although true solutions pass readily, colloids may go through slowly and particulate matter does not pass at all. The flow is through the foramen of Monro to the third ventricle and from here through the foramen of Magendie and the foramina of Luschka through the cisternae, which lie in the subarachnoid space. Here it is absorbed by the blood stream in the venous sinuses (sagittal, transverse, and

cavernous), through the arachnoidal villi, due to the greater osmotic pressure of the blood, the higher hydrostatic pressure in the subarachnoid space, and the thinness of these membranes. A small amount of cerebrospinal fluid is absorbed by the true lymphatics along nerves and blood vessels and also by the capillaries of the pia arachnoid similar to that of fluids elsewhere in the body. This is the fluid circulation of the brain and spinal cord and is the only one except the blood, for there are no demonstrable lymphatics in the brain, although there are some in the perineural spaces. The brain is guarded against excessively high blood pressure by the carotid sinus mechanism at the "vascular gateway." Changes in velocity supply more blood and O_2 per minute—great increases in volume do not normally occur in the cranial cavity which is closed. About 800 c.c. of blood pass through the brain each minute. The cerebral circulation must be kept constant. Wide fluctuations must not occur and therefore vascular regulation falls upon the liver and spleen (Chapter 22) and kidneys (Chapter 23).

There is much controversy concerning the physiology of the cerebrospinal fluid. This is particularly true concerning its mode of production.

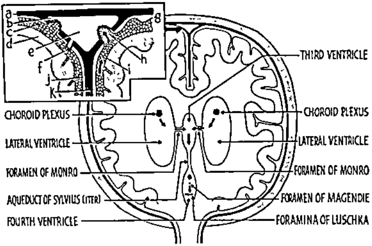

Fig. 202.—Circulation of cerebrospinal fluid. Diagram illustrating the ventricles of the brain and the circulation of the spinal fluid. The fluid is produced by the choroid plexuses in the lateral ventricles and passed through the foramina of Monro (*interventriculars*) to the third ventricle and thence through the aqueduct of Sylvius (*iter, or aqueducts cerebri*) to the fourth ventricle, where more fluid is added by a choroid plexus. From here the fluid flows through the median foramen of Magendie (*appertura medialis ventriculi quarti*) and the foramina of Luschka into the cisterna magna and then into the subarachnoid space of the spinal canal. Here there are some addition to the fluid (from cells) and some absorption through arachnoidal villi. Then the fluid returns to the cerebral subarachnoid space through other cisternae. Absorption takes place into the blood stream because of the greater hydrostatic pressure of the cerebrospinal fluid and the higher osmotic pressure of the blood. There are normally about 60 to 150 c.c. of fluid which contains 16 to 35 mg. of protein (as compared with 6300 to 8500 mg. in blood plasma). *a*, dura mater; *b*, parasinoidal sinus; *c*, subarachnoid space; d, cerebral cortex; *e*, superior sagittal sinus; *f*, cerebral vein; *g*, arachnoid mater; *h*, arachnoidal villus; *i*, pia mater; *j*, subdural space; *k*, falx.

The cerebrospinal fluid forms a column without valves about 600 mm. long in the average man. Its hydrostatic pressure is about 10 mm. Hg (lying down). The cerebral sinus pressure is about 6 to 8 mm. Hg, and the latter varies with the former. The blood pressure in the cerebral arteries is about 100 mm. Hg systolic and 65 mm. Hg diastolic. The capillary pressure is about 13 mm. Hg. On standing, the venous pressure may be zero. Changes in pressure in the right auricle are transmitted to the jugulars and so to the intracranial veins. Also respiration affects the intravenous pressure, causing an increase during expiration and a decrease during inspiration.

The osmotic pressure of the cerebrospinal fluid is not definitely known. Teschler and Fremont Smith say that the cerebrospinal fluid is in osmotic equilibrium with the

blood. Freezing points of blood serum and cerebrospinal fluid are the same. Hamilton states that the total electrolyte concentrations of serum and spinal fluid are the same.

Plasma exerts an osmotic pressure against isotonic salt solution in equilibrium with it of about 25 mm. Hg. Five millimeters of this pressure difference are due to the unequal distribution of electrolytes in accordance with Donnan's law and 20 mm. to the plasma proteins. Since the ependyma (ventricles and arachnoid) is impermeable to both electrolytes and proteins except at the tela choroidea, it is difficult to estimate such pressure in vivo and in vitro. Since the fluid resembles blood serum most closely, it is likely to have a comparable osmotic pressure. Although the protein content is low as compared with serum, it is not as important as in the blood capillaries because the electrolytes as well as proteins exert an effective osmotic pressure. This is due to the double membrane over the choroid plexus, making it less permeable to both. The osmotic pressure then is about 23 to 25 mm. Hg.

The osmotic pressure in the capillaries is about 25 mm. Hg and in the cerebral sinuses, 26 mm. Hg. Therefore, cerebrospinal fluid may reach the ventricles as a dialysate if it is in equilibrium with blood plasma or as an ultrafiltrate if the hydrostatic pressures are as depicted. The various pressures would be as follows:

	CEREBRAL SINUSES	C-SP. FLUID	CAPILLARIES
H =	13 mm. Hg	10 mm. Hg	6-8 mm. Hg
O =	25 mm. Hg	23-35 mm. Hg	26 mm. Hg

The osmotic pressure of lymph is about 18 mm. Hg, and its hydrostatic pressure varies with surrounding tissue space pressure.

Under normal conditions, then, *all attraction of fluid is toward the ventricles and then into the cerebral sinuses.*

This does not explain why cerebrospinal fluid will continue to form even in the face of increased intraventricular pressure. Since the pressure differences are so small and since the choroid is relatively impermeable to many substances, most observers believe the cerebrospinal fluid to be a secretion the direct product of the tela chorioidea. Flexner studied the problem on the basis of free energy change and concluded that the cerebrospinal fluid is to be considered a secretion; that is, the cells must do work in the formation of the fluid. Spinal fluid is reformed in three to five hours after it has been removed. The introduction of concentrated glucose into the venous system increases osmotic pressure within the venous sinuses and therefore attracts spinal fluid more quickly into them. Since fluid is attracted into the blood stream all over the body (see Chapter 11), the osmotic effect is soon lost.

Lumbar puncture reduces cisternal pressure in cases of increased intracranial pressure; at the same time the intraventricular pressure may remain disproportionately high, resulting in a temporary internal hydrocephalus. This may result in herniation of the medulla into the foramen magnum, causing embarrassment to the respiratory and cardiac centers.

Anomalies of the Skull and Meninges

Sometimes nature fails to close the skull and meninges at birth. This results in a protrusion of intracranial contents through the defect (cephalocele). It is usually in the median line, in the frontal or occipital region, or it may occur at the inner angle of the orbit. If the protrusion is composed of meninges and fluid, it is called a *meningocele;* if it contains brain tissue, it is known as an *encephalocele.* The treatment for these anomalies is surgical reduction and imbrication of the sac. In en-

cephalocele, due to the increase in intracranial pressure, the prognosis is guarded. In either case hydrocephalus may occur (see below).

Hydrocephalus is, as its name implies, an excess of cerebrospinal fluid within the ventricles (internal hydrocephalus) or in the subarachnoid

Fig. 203.—Infant with cephalocele (meningocele).

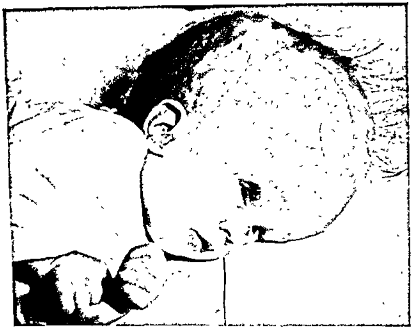

Fig. 204.—Congenital internal hydrocephalus. Note the flexed arms (this position is typical).

space (external hydrocephalus). The former is by far the more common and is either congenital (obstructions in the interventricular system) or acquired (obstructions due to new growths, meningitis, or arachnoiditis). We may well imagine that internal hydrocephalus could result from an overproduction of fluid. This is not the case, however, for

production is normal, but absorption is limited or absent. In any event, the cranial vault becomes enlarged, the sutures are widened, and the fontanels bulge. Whereas mild hydrocephalus is not incompatible with life or high mental development, the more severe types are. Such children rarely live over two or three years, and if they do, they are more or less helpless, mentally and physically. Treatment in the congenital types consists of needle puncture through the sagittal sinus into the subarachnoid space. External types of hydrocephalus are usually due to injuries or congenital anomalies and are localized. Their production is due to an interference of fluid absorption by the pia arachnoid capillaries in the involved area.

Function of the Brain

The brain is the great "telephone exchange" for the many "lines" that carry messages to and from every nook and cranny of the entire body. Within itself there must not only be ingoing and outgoing

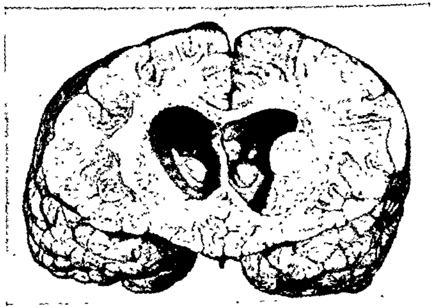

Fig. 205.—Internal hydrocephalus in a 19-year-old child, due to blockage of the aqueduct of Sylvius. The primary tumor was in the midbrain.

stations, but there must be communications between these. Also, the so-called silent areas, which may be termed the storehouse of impulses (memory) and perhaps of emotions as well, must be in intimate touch with the entire system. Nor is this all, for the autonomics (sympathetics and parasympathetics), although altogether outgoing and not under voluntary control, are nevertheless affected by all other divisions of this complex system and in turn may profoundly affect all other "departments."

The brain, then, receives impulses through the sensory nerves, which relay them to the afferent or sensory (dorsal and lateral) tracts in the white matter of the spinal cord, which in turn "deposit them" in the parietal lobes (post-Rolandic area) of the brain. This informs the body

of all of its contacts with the outside world, pleasurable or otherwise, and of its muscular movements (deep sensations). The senses of sight, smell, taste, and hearing are carried to the occipital, frontal, and temporal lobes, respectively, by special nerves (the cranial nerves, q.v.). Some of these impulses will be *stored in memory, others will be relayed to* special centers; still others may evoke responses in the higher centers of emotion or in the autonomies. Most of the impulses will be relayed to the frontal lobe (pre-Rolandic or motor area). From here they will go down the cord (anterior and lateral tracts) to find expression in voluntary movement. The coordinated muscular movements are controlled also in an involuntary manner through the cerebellar tracts, which carry impulses to the cerebellum from which messages are relayed to the motor area. Therefore, roughly, there are nerves that are sensory (telling us of our outer and inner contacts, or sensations); then there is a system that acts or responds to these stimuli in a voluntary way (muscle action) or involuntary way (autonomic action; then there is a coordinating muscle system that allows us to move and act. All of the systems intercommunicate so that there may be immediate action when necessary. Or the impulses may be stored for future use in the great memory zones (knowledge), where they may be unified, rearranged, and synthesized in a logical manner (learning or wisdom), thereby elevating man, *Homo sapiens,* above the mental level of lower animals.

Routine actions which do not need the help of the brain are handled in the spinal cord as *reflex actions.* These, together with special functions of the peripheral nerves, are discussed later in this chapter.

Areas of Localization

It is but a short time since modern surgeons first dared to enter the cranial vault—yet the operation of trephining is ancient. Research has made it possible to locate the functional areas of the brain. These cannot be definitely outlined, for the boundaries shade off into surrounding zones, but the areas are known sufficiently accurately to explain the physiology of normal activities and the symptoms and signs of pathological ones. The following areas are recognized:

Frontal Lobes.—

1. Motor area (precentral gyrus—pre-Rolandic area)—muscle movements.

2. Silent area—memory, orientation, emotional control, and association of ideas. Especially the left frontal lobe. Prefrontal lobotomy is done in those who lose *their normal traits.*

Parietal Lobes.—

1. Sensory area (postcentral gyrus—post-Rolandic area).

2. Somesthetic area, or stereognostic areas—spatial recognition, recognition of relative intensity, recognition of similarity and difference. If diseased, astereognosis results.

Temporal Lobes.—

1. Centers for taste and smell.

2. Optic tracts sweep by. When a tract is injured, hemianopia results.

3. Auditory area, with speech center on left side in right-handed people. They are said to be "left-brained." Lesions here produce sensory or motor *aphasias*. In addition, lesions of the temporal lobes may produce auditory, olfactory, and gustatory disorders. There may be dreamy states and disturbances of memory; sometimes epileptiform seizures which are preceded by aura of smell, taste, or hearing.

Occipital Lobes.—

1. Visuosensory area.

2. Visuopsychic area—visual sensations interpreted.

3. Memory images of speech are located here. If the area is diseased, *alexia* occurs (inability to read although letters and words are seen). Motor speech is preserved and understanding is unimpaired.

The most important from the standpoint of the surgeon are the pre-Rolandic and post-Rolandic areas. The pre-Rolandic area is a motor area, with the center for the muscles of the face at the lowermost (inferior) portion of the anterior central gyrus and the center for the muscles of the extremities at the superior limits of the gyrus. The post-Rolandic area is a sensory area and, if diseased, precludes or alters such stimuli as occur from pain, heat, cold, etc.

Cerebellar lesions produce *ataxia,* lack of muscle sense, staggering gait, and hypotonia of the muscles.

Diseases and Injuries of the Brain

Pressure Symptoms.—Symptoms and signs of brain disease arise principally from an *increase* in *intracranial pressure.* These are known as *pressure symptoms.* They vary not only with the degree of pressure, but also with the rapidity with which they occur. Thus in cranial injuries where the increase in intracranial pressure is sudden, symptoms will be severe and ominous, whereas the same degree of pressure evolved slowly will evoke only moderate symptoms. This is due to adjustments of tissues to a diminishing blood supply compensated by collateral vascularity where possible and decreased tissue metabolism. This same observation pertains to any organ or tissue as illustrated in gradual occlusion of the common carotid, hepatic, and abdominal aorta with minimal changes in the brain, liver, and lower extremities as opposed to abrupt interruptions with resulting necroses. The triad of symptoms upon which diagnosis is most commonly made is headache, vomiting, and a choked disc. Other symptoms are less constant.

1. *Headache* is severe and intractable (organic headache). It may ameliorate at times but does not disappear.

2. *Vomiting* is unrelated to food and is usually projectile in type.

3. A *choked disc* results from an interference with the venous return and *the circulation of the cerebrospinal fluid. There is an edema of the* optic nerve head, papilledema, which obliterates its margins. This is seen through the ophthalmoscope and is an invaluable sign.

4. A less constant pressure symptom is a *change in the reflexes.* This is always present in motor area disease. Often the growth may *stimulate*

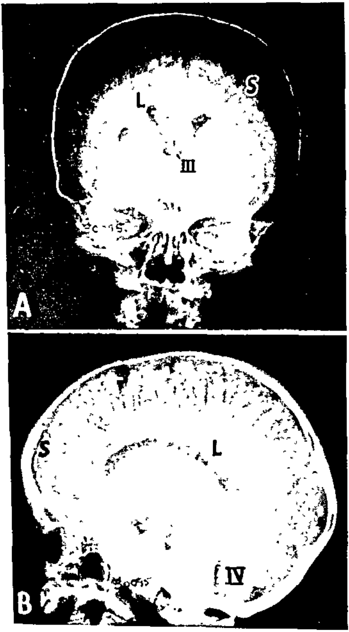

Fig. 206.—*A*, Encephalogram visualizing the lateral ventricles (L), the third ventricle (III), and the subarachnoid space (S). *B*, Encephalogram visualizing the lateral ventricle (L), the fourth ventricle (4), and the subarachnoid space (S). Air was injected into the subarachnoid space through lumbar puncture.

by local irritation the motor zone, producing *convulsions* or *spasms*, either in one set of muscles (jacksonian contractions) or over the entire body.

5. The function of the brain may be so *depressed* as to produce *paralyses*. These are usually limited but may involve a whole side of the body. These symptoms and signs suggest brain disease. By studying them carefully, together with the more definite localizing signs which may be present, the location of the area involved may be surmised. In addition, such measures as *ventriculography* (injection of air into the ventricles and x-ray), spinal and cisternal punctures for pressure reading, and cell counts, protein, and sugar content help determine the presence and position of growths. At operation a more precise location of cerebral tumors may be obtained by means of radioactive phosphorus and a special Geiger-Müller counter (Selverstone and associates).

Head Injuries.—The most common injury to the head is a contusion, with or without skull fracture. If the scalp is lacerated, it will demand the same treatment as has previously been described for other wounds. However, the hair must be carefully shaved. Bleeding is profuse, because of the arrangement of vessels in the subcutaneous layer. The important consideration is not the scalp wound, or the extent of the fracture, which may be present; it is the probability of injury to the brain.

Classification of Fractures of the Skull.—Classification is necessary to explain certain symptoms and signs and types of treatment. The fracture per se is relatively unimportant and will heal; the injuries beneath the skull (in the brain) determine the outcome of the injury.

A number of different criteria are used for the classification of skull fractures:

1. Method of production; most fractures of skull result from tension that is tearing apart rather than compression
   a. Bursting fracture (skull squeezed between two objects)
   b. Indented fracture (skull fractured by blunt force)
   c. Penetrating fracture (skull fractured by a bullet or sharp instrument)
   d. Expansile fracture (skull fractured by a bullet or explosive which causes expansion as it passes through the head)

2. Nature of the break
   a. Fissured (single line)
   b. Comminuted (many radiating lines)
   c. Depressed (skull is dented)

3. Anatomic location
   a. Base
      (1) Anterior fossa
      (2) Middle fossa
      (3) Posterior fossa

b. Vault
   (1) Frontal region
   (2) Parietal region
   (3) Occipital region

4. Degree of injury to overlying scalp
   a. Simple
   b. Compound

Cerebral Compression.—The brain lies in a rigid case. When swelling or extravasation occurs, brain tissue becomes compressed. When it is squeezed, it loses its blood supply, and anemia of the brain follows. This is known as *cerebral compression.* Its chief causes are (1) edema, (2) hemorrhage, (3) inflammation or suppuration, (4) new growths, (5) foreign bodies.

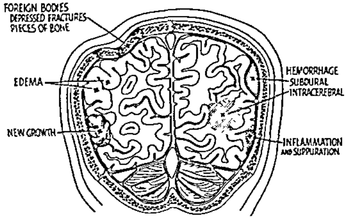

Fig. 207.—Diagram illustrating some causes of cerebral compression. The acute types are caused by hemorrhage, or edema, or both) or by foreign bodies; the less acute, by inflammation; and the chronic, by new growths. Symptoms appear immediately in the acute type, late in the chronic types.

These causes may be present singly but as a rule it is a combination of morbid changes that produces cerebral injury and compression. Swelling is more often due to blood than edema. In fact, the latter is difficult to demonstrate at necropsy and there is actually often less fluod in a traumatized brain than in a normal one.

Acceleration and deceleration of the head and direct compression by deformation of the skull may result in increased intracranial pressure waves. Deceleration is due to indirect injury. Mass movements of the brain occur when the head is free to move. Oxidative processes are about normal in injured brains except in areas of contusion and laceration. This is also true in simple depressed fractures where pathological changes are caused by the original blow and not by irritation of the overlying depressed bone.

Contrecoup or indirect injures imply that the brain may be injured on the opposite side of the point of impact. Injuries to the brain on the

same side of the external blow are known as coup injuries. These injuries to the brain may occur without influence of skull fractures, especially when the head in motion strikes a stationary object. The lesion is not always directly opposite to the impact. Since the occipital region is rarely involved by contrecoup damage, the anatomical relation of the brain and the portion of the skull proximate to it is probably responsible for the nature and distribution of the lesion. The mechanism is probably a wave of force transmitted directly through the brain, thrusting it to the opposite side and producing injuries along the route of this force. When blood does not reach the brain, its function is severely impaired in the higher centers and also in the medulla. This impairment will be greater in conditions which come on rapidly and less severe (though equally disabling) in new growths which grow slowly enough to allow the brain to adjust to the increasing pressure.

Degrees of Cerebral Injury.—The following injuries may occur: (1) *Concussion*—a shaking-up of the brain, with little or no organic change; that can be grossly demonstrated. However, significant alterations in arrangement, shape, and size of Nissl bodies have been observed in experimental animals, without showing any change in nerve fibers or myelin sheaths. In less than twenty-four hours after concussion, chromatolysis of certain neurons begins (chiefly the lateral vestibular nuclei and the large neurons of the tegmentum of the midbrain, pons, and reticular formation of the medulla oblongata). In two days many cells showed great changes which progressed to complete destruction by the eighth day, and these changes were different from those observed after sectioning a nerve or in anoxia. Primary afferent and primary efferent neurons of the cranial ganglia and cranial nerve nuclei are not often affected. Hemorrhage is not encountered but some observers report changes characteristic of anoxemia. This, coupled with a rise in intracranial pressure above systolic pressure (in dogs), may explain mild cases of "punch drunkenness" or severe cases of concussion coma. (2) *Contusion*—a severe blow to the brain, producing a rupture of the smaller vessels, with resulting edema and hemorrhage. (3) *Laceration*—a tearing of the brain tissue, with injury to nerve cells and much hemorrhage. (4) Combinations of the foregoing.

Symptoms and Signs.—The symptoms produced will vary with the degree of cerebral injury or compression.

When a patient sustains a severe head injury, he may first go into a state of shock (see Chapter 14). Later he will react from this state, and as intracranial pressure increases, his vital centers will be stimulated. If this pressure continues, the vital centers will become inhibited, but if it ameliorates, they may return to their normal activity. Careful and close observation of the patient will reveal the degree of injury, the prognosis, and indications for treatment. The following information is vital: (1) state of consciousness; (2) sphincteric control; (3) tempera-

ture; (4) pulse; (5) respiration; (6) blood pressure. This information should be carefully charted at half-hour intervals so that trends may be evaluated.

1. *Stage of Shock:* If shock is profound, there may be unconsciousness and lack of sphincteric control. Usually this is not true. It is difficult to separate concussion and contusion of the brain from cerebral shock. In civilian practice shock is commonly encountered due to brain injury or associated trauma (see Chapter 14).

The temperature in shock will be subnormal. The pulse will be rapid and thready (130-150). The respiration will be shallow and rapid (30-40). The blood pressure will be low (90/40).

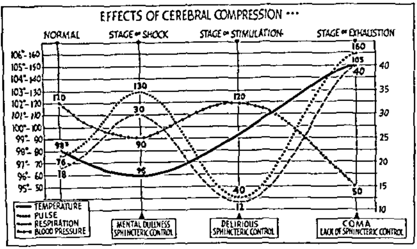

Fig. 208.—Effects of acute cerebral compression as seen after skull fracture. The patient is usually brought to the hospital in a state of shock. After one to two hours there is a reaction, with symptoms of cerebral compression. These are at first stimulated to the vital centers, but if pressure continues the centers fail.

2. *Stage of Reaction:* Soon there will be a reaction, and if intracranial pressure is increasing, the vital centers will be stimulated in an attempt to keep pace with the increase. The cardioinhibitory center will be stimulated (bradycardia) and the pulse will be very slow (40 to 60) and regular. The respiratory center will be stimulated and respirations will be deep, slow (12-15), and regular. The vasomotor center will be stimulated and the blood pressure will go up say to 120 systolic over 80 diastolic. In addition, the higher centers may be stimulated, making the patient restless and delirious.

3. *Stage of Depression:* If the intracranial pressure continues to increase, the centers become depressed and finally paralyzed. This is due to the fact that this pressure ultimately equals the systolic blood pressure (because of a decreased absorption by the occluded venous sinuses and increased filtration from the choroid plexuses), and this prevents blood from reaching the brain. The cardioinhibitory center will not exert its control, and the pulse will become rapid and irregular. (Great variability in

pulse rate is a bad prognostic sign.) The respirations will be shallow, rapid, and irregular, or Cheyne-Stokes in type.

Cheyne-Stokes respiration in increased intracranial pressure has been explained by Cushing as follows: When the increase in intracranial pressure is greater than the arterial blood pressure, there results an anemia of the brain which suspends the activity of the respiratory center. At first this increased intracranial pressure stimulates the vasomotor center, causing a rise in blood pressure, which causes a more rapid flow of blood to the medulla and resuscitation of the respiratory center. This steplike series of increases gives rise to the period of breathing and cessation of breathing. No doubt the accumulation of CO_2 aids in stimulating the respiratory center. Henderson believes that the periods of deep breathing may cause a diminished CO_2 (acarbia) in the blood. Acarbia causes not only apnea, but also rapid heart beat, fall in blood pressure, and shock. Perhaps CO_2 may be necessary to keep up the normal irritability of the vasomotor center.

The respiratory center is normally under the control of:

1. Chemical influences. Carbon dioxide is probably the controlling factor; however, lack of oxygen may excite the center also. In Chapter 12 we have seen that the pH of the blood may influence the center. Carbon dioxide excess increases chiefly the *depth* of breathing.

2. Nervous stimuli.

a. These are carried chiefly by the vagi, which act to offset any changes in respiration. When the lungs are distended with air, afferent vagal impulses inhibit the automatic action of the center and arrest inspiration, thereby bringing on expiration; when the lungs are empty of air, these impulses stop, thereby arresting expiration and permitting inspiration to occur (Hering-Breuer reflex). Therefore, the vagi influence both the *rate* and *depth* of breathing.

b. Sensory stimuli for any portion of the body carried over sensory nerves may have a *pressor* effect, causing quicker and stronger inspiration, or a *depressor* effect, causing respirations to become slower, or more feeble, or even to cease entirely.

c. Voluntary control may be exerted over respiratory movements.

d. Carotid sinus impulses arise from changes in blood pressure. A low oxygen content of arterial blood may stimulate the center. CO_2 affects the carotid body as do oxygen lack and H ion concentration. As arterial pressure rises, depth of respiration decreases, and if it continues, there is apnea.

Blood pressure will fall rapidly and progressively. As increase in intracranial pressure occurs, the temperature increases. This is difficult to explain, but it is probably due to an injury of the heat-regulating center. If the patient has no control of the sphincters, and has lost consciousness, lying in a stupor or coma, the higher centers are also paralyzed. Should the intracranial pressure decrease, the blood pressure,

pulse, respiration, temperature, and mental state will return toward normal. This information is far more valuable than that obtained from spinal punctures (which may increase the bleeding) or from x-rays, which may be done later, as a matter of record.

Prognosis.—Seventy per cent of all head injuries will get well if treated expectantly. Twenty per cent will die in spite of anything we may do because of extensive brain lacerations. Ten per cent need active aid.

Treatment of Head Injuries.—The patient should not be moved to be x-rayed for two or three days. The reason is that moving him may increase the shock and finding the fracture offers little help in treatment. It should be done before the patient leaves the hospital. Also, lumbar punctures should not be done. There has been much argument about the value of this. If the brain is torn and bleeding, and if it is being carefully compressed by the cerebrospinal fluid, lumbar puncture will relieve the compression but is apt to increase the hemorrhage, or further traumatize the brain by causing it to jam against the foramen magnum, or increase the shock.

Spinal fluid pressure is an indicator of cerebral compression. However, there may be great elevations in pressure with little interference with function and therefore few symptoms, or there may be small increases in pressure with much interference of function and many symptoms. In a way, spinal fluid pressure is comparable to the systemic blood pressure in this regard. Consequently, a careful study of cerebral symptoms is perhaps more important than the knowledge of cerebrospinal pressure. The presence of blood implies serious brain injury and this is easily ascertained by the symptoms and signs. Large doses of morphine or barbiturates should not be given, for these drugs decrease and depress the respiration and clouds the clinical picture, so that it may be difficult to determine whether the patient is in a state of unconsciousness or not. If restless, the patient may be given small doses of rectal ether or, better yet, paraldehyde, 10 to 20 c.c., per rectum. Hypertonic dextrose solutions, given intravenously, are advocated by many. However, Dandy, Masserman, and others oppose its use. Glucose and sodium chloride are stored in the brain. Sucrose is rapidly excreted and carries water with it. Opposition to the use of concentrated (50 per cent) glucose solution is based on the fact that it causes a primary fall in cerebrospinal pressure, followed by a secondary rise. There are also headache and adverse chemical reactions in the brain. Also hypertonic solutions are known to produce foamy swelling of the lining cells of the renal convoluted tubules. Some believe that edema is actually increased. In Chapter 11, The Interchange of Body Fluids, we have observed that fluid is drawn into the blood stream by hypertonic solutions. This temporary hydremia is relieved by increased diuresis, with a net loss of water to the body, thereby further increasing the density of the blood. Thus more fluid is removed from the tissues and consequently more from the cerebrospinal

fluid. Ultimately dehydration of the brain will occur. Dehydration reverses pressures in the cerebrospinal fluid and blood, lowering the former below the latter. This would cause any fluid produced by the choroid plexus to be promptly absorbed not by hydrostatic but by osmotic factors. Thus the ventricles are rendered empty for variable periods, theoretically permitting the brain to expand.

Brain cells need salt, glucose, and oxygen for their metabolism. If dehydration produces a stagnant anoxemia, as it usually does, there will result cerebral anoxia and increased permeability to uninjured, as well as to injured capillaries. The injured leaky capillaries, however, may permit the hypertonic solutions to enter the intercellular spaces and thereby produce more edema. Filtration and absorption in the brain may be explained in part by Starling's theory. After trauma, there is capillary dilatation with leakage of plasma. This in itself draws cerebrospinal fluid into the intercellular spaces. Since no lymph spaces are present, absorption must occur through the arachnoidal villi into the cerebral sinuses. Stasis occurs due to venous compression and causes more plasma to leave the vessels, thereby increasing the edema.

Perhaps a better plan of treatment than the use of hypertonic glucose is repeated transfusion of blood plasma, which has a higher osmotic pressure and will not leave the capillaries so readily. This may cause a more rapid absorption of the cerebral edema. Dehydration is not produced either by withholding fluid or by using hypertonic solutions, nor is hydremia induced by too much fluid. We usually give 500 c.c. of physiological saline by hypodermoclysis, 500 c.c. of 5 per cent glucose in distilled water intravenously during the course of twenty-four hours in an adult of average weight. We are governed by the same factors of hydration as set forth in Chapter 11 plus signs of intracranial pressure plus indications for whole blood as determined by the hematocrit and plasma protein determinations which, though transient signs, are helpful guides. Drugs are used to relieve pain and induce rest but must not be strong enough to produce unconsciousness or depress the respiratory center, for death may occur from respiratory failure. If a patient lives eight to ten hours after the injury, he will probably recover.

Other aids in treatment include the following:

(1) Elevation of the head of the bed which reduces venous, sinus, and cerebrospinal fluid pressure and also allows for pooling of blood in the splanchnic area and lower extremities. This may reduce intracranial pressure.

(2) Administration of oxygen.

(3) Anchoring a catheter and recording hourly output and specific gravity. This is the most reliable sign for fluid requirements when used with other clinical signs of water balance as set forth in Chapter 11.

(4) Watchful inactivity—the guiding philosophy in most head injuries.

(5) No intravenous or subcutaneous fluid if the patient is conscious and can take the fluid and food by mouth.

The 10 per cent that require operative treatment are those with a compound fracture, those who have survived the first ten hours but in whom intracranial pressure is increasing, and, lastly, those who have a torn middle meningeal artery. The first group require careful débridement. The scalp should be shaved widely and the wound carefully cleansed with quarts of physiological saline solution. All foreign bodies are removed and the scalp is closed. The local use of sulfonamides is not recommended because of the foreign body reaction which may ensue. This is particularly true if the dura is exposed or has been torn. The second group require a subtemporal decompression to relieve pressure. Depressed fractures do not necessarily require operative interference. If the skull has been fragmented or spiculated with injury to the dura or when depression of the skull is over functioning cortical areas, producing symptoms, then the depressed fragments should be elevated. All defects of 3 to 5 cm. or more of the skull require some interference. They may be repaired by osteoperiosteal transplants from the outer table in small defects in young people. Large defects may be filled in with tantalum or methyl methacrylate. Exenteration of the mucous membrane of the frontal sinus and occlusion of the osteum of the vasofrontal duct is necessary to avoid potential sources of infection. The third group require a trephine opening to tie off the bleeding vessel. A line drawn 1½ inches behind and ½ inch above the external angular process will locate the site of this vessel. If it is torn, the patient will have a more or less definite set of symptoms. When a patient is first injured, he has a *concussion* or "shaking up" of the brain, producing mild, transitory symptoms. He "sees stars," loses consciousness, but soon recovers. If the middle meningeal artery is torn, he soon loses consciousness again, due to hemorrhage and an increase in intracranial pressure. A *period of consciousness between two periods of unconsciousness means a torn artery.* If it is a large tear, bleeding will be profuse and consciousness will be short. If it is a very small tear, the patient may remain conscious for three or four hours, or even longer. There will be a dilatation of the pupil on the same side due to pressure on the oculomotor nerve inactivating it. This is not always present. A *subdural* hematoma is usually venous and is more apt to produce dilatation of the pupil and paralyses with irritability (like a frontal lobe tumor). Subarachnoid hemorrhage is more apt to produce irritative and general symptoms.

Penetrating and perforating wounds require x-ray examination to determine the presence of foreign bodies. These wounds may be closed after careful débridement except in cranio-orbital and frontal sinus wounds where later repair is preferable because of infection. Metallic bodies should be removed if possible because they may lead to secondary abscess and convulsions (epilepsy). The defect in the dura should be

closed promptly and completely in clean wounds by primary suture or if too large a defect, by periosteal or fascial grafts.

A good rule to follow is: All head injuries must be carefully observed, preferably in the hospital, for at least forty-eight hours.

In fractures of the base of the skull, there may be bleeding from the nose, or ecchymosis under the eyes (anterior fossa), or bleeding from the ears (middle fossa), or ecchymosis behind the ear (posterior fossa). This bleeding should not be controlled, for to do so may mean the introduction of infection in the brain covering (meningitis), and it stops nature's way of doing a decompression.

Complications of skull fractures may be divided into early and late. Early complications include (1) extradural hematoma, (2) subdural hematoma, (present in about 12 per cent), (3) ruptured eardrum, (4) foreign bodies (bone, metallic fragments), (5) infections inside the skull (meningitis, brain abscess), (6) infections outside the dura (osteomyelitis, cellulitis of the scalp).

Late complications and sequelae are (1) extradural hematoma, (2) convulsions (jacksonian); (3) headache, dizziness, pain in the temporal and occipital regions, (4) mild disturbances in mentality, nervousness, (5) aphasia, (6) hemipareses, (7) involvement of the first, second, third, fourth, sixth, and eighth cranial nerves. Many of these sequelae are due to arachnoidal adhesions or subdural hematoma or depressed fragment of bone. Diagnosis is made with difficulty and must be separate—the true case from the malingerer and the functional from the organic. X-ray studies, encephalograms, and symptoms and signs may lead to a focal area which may be explored. Sometimes an old clot beneath the dura is the cause. Its removal may result in complete cure. More often arachnoidal adhesions are found and separated—the results may be good but often are discouraging.

Epilepsy.—The term epilepsy is loosely used to mean any convulsion state, tonic, or clonic. Really epilepsy is not a disease entity but a symptom of vaguely understood brain dysfunction. There may be slight convulsions (petit mal) or prolonged convulsions (grand mal), with frothing mouth and tongue biting. The laity speaks of it as "fits." There is no specific treatment; however, phenobarbital, sodium diphenylhydantoin, insulin shock, acidosis, and even surgical intervention have been tried.

Jacksonian convulsions (jacksonian epilepsy) refers to focal motor convulsive seizures which most often affect the upper extremity. Although cicatrices and space-consuming lesions may produce the symptom complex, often no abnormality is demonstrable. The treatment may be by drugs (Dilantin sodium) or by surgery. The latter consists of electrical exploration to find the focal area involved (usually lower portion of anterior lip of central sulcus), then resection with the electrosurgical cutting current of the pia and superficial gray matter, and then by blunt dissection resection of the cortex to the depth of the central sulcus. Removal of tissue is usually confined to the precentral convolution.

Cerebral Complications Following Surgical Operations not Performed on the Brain.—These may be due to: (1) cerebral hemorrhage in older group; may be coincidental; (2) embolism in younger group especially; may occur in all age groups and is especially to be feared after chest operations, particularly lung abscess and empyema; (3) peculiar idiosyncrasy to anesthetic(?); (4) coma, tremors, and convulsions and psychic disturbances due to "toxic" psychosis, especially after thyroid operations; (5) "readjustment psychosis" thought to be due to sudden change from more to less sick state; (6) *cerebral anoxia* which produces most psychoses, comas, convulsions, and paralyses after surgical operations. This results from alteration in blood pressure, cardiac inadequacy, and anoxic anoxemia due directly to the anestheic or its administration. The cerebral changes are parenchymatous edema and congestion and perivascular fibrosis.

Brain Abscess and Sinus Thrombosis.—Brain abscess and sinus thrombosis occur usually from middle ear disease and mastoid infections. The abscess is usually in the temporal lobe; it evokes no fever because there is no absorption (absence of lymphatics and looseness of tissue). Drainage is done by needle aspiration after complete localization. However, better results follow surgical drainage. The mortality, including complications, is about 40 per cent. Sinus thrombosis is simply a phlebitis of the lateral sinus. The treatment is conservative as in phlebitis elsewhere but includes the use of penicillin and sulfadiazine.

New Growths.—New growths such as *gliomas, hypophyseal adenomas, meningiomas,* and *neuromas occur.* They may be encapsulated and therefore easily removable or infiltrative (gliomas) which defy extirpation, although some of these have been successfully removed. More than half of all brain tumors may be successfully removed if seen early. Most tumors in adults occur above the tentorium, except the cerebellopontine angle tumor or perineural fibroblastoma of the eighth (auditory and vestibular) nerve. Most brain tumors in children are of the cerebellum or below the tentorium, except epithelial cysts near the pituitary (Rathke's pouch cysts, craniopharyngioma). *Gliomas* make up 50 per cent of all intracranial neoplasms and include all types of glial cells in their various stages of embryonic growth and development. *Astrocytomas* make up about one-fourth of gliomas. There are three subtypes: (1) fibrous (piloid or pilocytic) astrocytomas which are composed of cells rich in fibers; this type carries best prognosis; (2) protoplasmic (diffuse) astrocytomas seen in cerebrum with infiltrating cells; tumor limits poorly defined; responds to x-ray; (3) Gemistocytic astrocytoma which is composed chiefly of Nissl's plump cells; most rapidly growing and is the most unfavorable. *Glioblastoma multiforme* (spongioblastoma multiforme) originates in the white matter but is very invasive and usually grows rapidly; unless it is removed very early, it cannot be entirely removed. *Medulloblastoma* is the commonest type of glioma in childhood. It arises in the cerebellum

and early involves the fourth ventricle and other areas because of its friability and early cellular desquamation. It is radiosensitive. *Cerebellar sarcoma* resembles medulloblastoma and involves the cerebellum in older persons. *Ependymomas* occur in the brain and spinal cord and have connections with the ventricular system. They grow slowly, are firm, as a rule, and may be removed if in a favorable position. They are radioresistant. *Polar spongioblastoma* (spongioblastoma polare) is another type of glioma seen in the pons, optic chiasm, and corpus collosum. The tumor is invasive and usually defies extirpation and is not radiosensitive. *Oligodendroglioma* is a form of glioma which grows slowly and is firm. It occurs in the cerebrum and is difficult to remove and is radioresistant.

Meningiomas make up about 16 per cent of brain tumors. They are seen usually above the tentorium and therefore affect the cerebrum more frequently than the cerebellum and brain stem. They usually arise in the arachnoid but may invade the skull and are often attached to the dura. They are usually not invasive, pushing the brain aside, although they are vascular and do invade the cerebral sinuses. The prognosis is good because complete extirpation is possible, although this may require several stages. *Cerebellopontine* angle tumor (eighth nerve tumor, perineural fibroblastoma of the eighth nerve; acoustic neuroma) arises from the perineurium of the eighth nerve just at the porus acusticus. It is usually encapsulated and may be completely removed, producing a cure. *Pituitary tumors* (see Chapter 22.) *Chromophobe* adenomas cause local signs (bitemporal hemianopsia) and endocrine disturbances such as progressive reduction of sexual function. *Eosinophilic* adenomas cause acromegaly. *Basophilic* adenomas are not usually of surgical importance. Adenomas are sometimes cystic. Early excision is feasible.

Tumors of the hypophysial duct (Rathke's pouch cyst, craniopharyngioma, pituitary admantinoma) are slowly growing, usually cystic. They produce delayed sexual development and after puberty they alter this function. If they press on structures in the region of the third ventricle, metabolic changes, obesity, and dwarfism may be produced. They occur early in life, are often calcified, and although not easily removed, the cysts may be emptied, giving relief or symptoms.

Epidermoid and *dermoid cysts* (cholesteatoma, pearly tumor) are found in the third ventricle, posterior fossa, and in the skull itself (lateral margin of orbit). They occur early in life and give evidence of their presence by pressure symptoms. If they cannot be removed, they may be drained, relieving symptoms. *Vascular tumors:* (1) *Angiomas* are congenital malformations (see Chapter 17) and in the brain are classified as telangiectases or venous and arteriovenous angiomas. Sometimes they produce convulsions by causing a scarring or by hemorrhage. They may become calcified and thus may be seen by x-ray. The arteriovenous fistulas often produce a discernible bruit and the "swish" may be heard by the patient. They should be removed if possible. Sometimes ligation of

principal vessels produces relief. (2) *Hemangioblastoma* is a tumor of proliferating blood vessels and endothelial cells. It is usually found in the posterior fossa and may be cystic. Rarely there is an associated angioma of the retina and cystic degeneration of the liver, kidneys, and spleen (Lindau's disease). X-ray therapy may help if removal is not feasible. *Metastatic tumors* may come from the thorax, retroperitoneal region, and breast and malignant melanoma from anywhere. Cancers of neck and throat may invade by direct extension. A single lesion may be removed to give relief, just as a single metastasis to the lung may warrant a lobectomy.

Even *tuberculomas* or *gummas* may give the classical symptoms and signs of brain tumor. Whether removal is necessary or not, the surgeon will perform a *decompression* (subtemporal, usually) to reduce the intracranial pressure and thereby relieve the headache and save the sight until the growth is reduced by radium or (when caused by tuberculosis or syphilis) by medication (streptomycin in tuberculosis and penicillin in syphilis). Schistosomiasis japonica may also invade the brain (see Chapter 7).

Cerebral hemorrhage in the newborn results when the veins of the tentorium are torn. Often it is due to a hemorrhagic diathesis in the child (Rh factor, erythroblastosis). Transfusion is the best treatment in addition to vitamin K.

THE SPINAL CORD

The spinal cord lies within the vertebral column and extends from the brain, or rather medulla oblongata, to the second lumbar vertebra although the dura and arachnoid extend down to the third sacral vertebra. A lumbar puncture is done at the level of the iliac crests; that is, between the third and fourth lumbar vertebrae, thus avoiding injury to the cord. Some prefer the interspace between the last lumbar and the first sacral, especially for the inexperienced. The reason is to avoid injury to the posterior part of the annulus fibrosus, thereby predisposing to herniated nucleus pulposus. The cord ends in a group of nerve fibers called the cauda equina. The peripheral portion of the cord is white and is made up of ascending (sensory) neurons and descending (motor) neurons. The central portion is gray and is composed of nerve cells. The various tracts are indicated in the diagram.

The *medulla oblongata* lies just above the foramen magnum, through which the cord emerges. Here lie the important respiratory, cardiac, and vasomotor centers. A sudden jamming of the medulla into the foramen magnum may produce death. Therefore, lumbar punctures are done with the patient lying on his side. In a patient with increased intracranial pressure, a lumbar puncture should be done with extreme caution, if at all.

The simplest cord function is the spinal reflex, which is mediated by an afferent or ingoing neuron, entering the cord by the dorsal root; a connector neuron within the cord; and an efferent or outgoing neuron, leaving the cord by the anterior root. Some tracts cross high in the cord (the pyramidal tracts), some at various levels (the sensory fibers for pain and temperature). The cord is roughly distributed to different zones of the body. The first costal interspace marks the boundary between the fourth cervical and the second thoracic zones (most nerves from this region go to the arm); the region of the nipple line is innervated by the fourth thoracic nerves; the umbilical region, by the tenth thoracic nerves; the pubic, by the twelfth thoracic nerves; and the anal

region by the third, fourth, and fifth sacral nerves; the lower legs are innervated by the lower lumbar and first two sacral nerves (Homans).

Since the spinal column "grows away" from the cord in its development, the segments of the cord are not at the level of the corresponding vertebrae. There are eight cervical pairs of spinal nerve roots, twelve thoracic, five lumbar, and five sacral. Since the cord ends at the second lumbar vertebra, the five sacral nerves and the three lower lumbar lie above this point. The lower thoracic and upper lumbar segments will be found three vertebrae higher; the upper thoracic and lower cervical, two vertebrae higher; and the upper cervical, one vertebra higher. In other words, pain originating in the pelvis (level of third lumbar vertebra) is referred to the twelfth thoracic segment by way of the iliolingual nerve (T 12 and L 1).

Each spinal segment supplying a peripheral zone makes possible sensation, movement, reflex movement, and autonomic control. Therefore, in cord lesions of any kind, a disturbance of any or all of the above functions may be expected. Sensory changes may manifest themselves as *paresthesia* (numbness), *hypesthesia* (decreased sensation), *hyperesthesia* (pain from touch), or actual *pain*. Crossed paralyses of *Brown-Séquard* are seen in patients with tumors which press on one side of the cord only. Pressure on the lateral pyramidal (decussates in medulla) will cause muscle weakness on the same

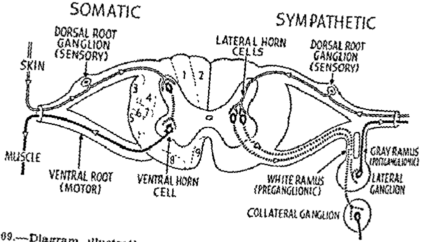

Fig. 209.—Diagram illustrating cross section of spinal cord. On the left are the somatic, and on the right, the sympathetic nerves. The neurons (efferent, connecting, and afferent) necessary to complete a simple reflex are shown. *1* and *2*. Fasciculus gracilis (Goll) and fasiculus cuneatus (Burdach). These are the sensory spinobulbar tracts (tactile and kinesthetic impulses). *3*. Cerebellar tract (direct coordination). 4. Corticospinal crossed-pyramidal, or motor tract (voluntary motion). *5*. Spinothalamic tract of the lateral column (pain and temperature). Fibers arise in the posterior ganglion of the opposite side and cross in the anterior commissure. *6*. Cerebellar tract (indirect coordination). 7. Rubrospinal tract or crossed-motor tract aids the pyramidals. 8. Spinothalamic tract of the anterior column (tactile sensation). Fibers arise in the posterior ganglion of the opposite side. 9. Corticospinal, or direct pyramidal tract (voluntary motion). The preganglionic fibers of the sympathetics are shown by the dotted line; the postganglionic fibers, by the black line (See Fig. 202.)

side, whereas pressure on the posterior columns (also decussates in the medulla) will cause diminution of common sensibility and sense position (kinesthesia) on the same side, producing a tabetic form of ataxia, or if above the level of the brachial plexus, astereognosis as well. However, when pressure exists on the anterolateral columns there will be a disappearance of pain and temperature sense on the opposite side because these tracts cross over at the anterior commissure after they enter from the posterior root ganglion. In syringomyelia or hemorrhagic or other lesions of the central part of the cord, pain and temperature sensations are absent, tactile sense remains. Cordotomy to relieve pain is done here. Motor changes may be flaccid paralysis (from injury to anterior horn cells or to the lower motor segment, as in *anterior poliomyelitis*), or spastic paralysis, or hyperflexia (from injury to the upper motor segment), when the long tracts are irritated as in hemorrhage, injury, etc.

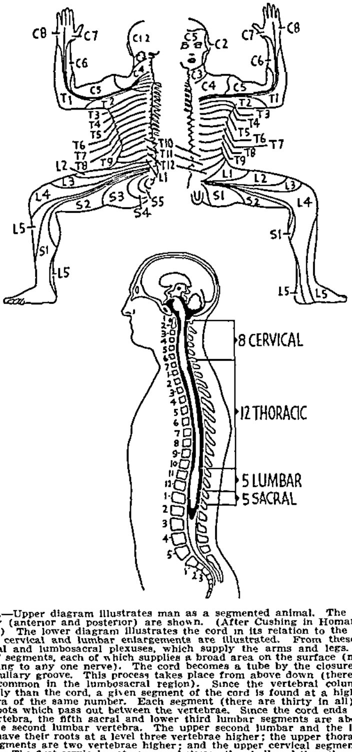

Fig. 210.—Upper diagram illustrates man as a segmented animal. The sensory zones of the body (anterior and posterior) are shown. (After Cushing in Homans: Textbook of Surgery.) The lower diagram illustrates the cord in its relation to the vertebral column. The cervical and lumbar enlargements are illustrated. From these areas come the brachial and lumbosacral plexuses, which supply the arms and legs. The cord is made up of segments, each of which supplies a broad area on the surface (not necessarily corresponding to any one nerve). The cord becomes a tube by the closure of the edges of the medullary groove. This process takes place from above down (therefore anomalies are most common in the lumbosacral region). Since the vertebral column grows far more rapidly than the cord, a given segment of the cord is found at a higher level than the vertebra of the same number. Each segment (there are thirty in all) has its pair of nerve roots which pass out between the vertebrae. Since the cord ends at the second lumbar vertebra, the fifth sacral and lower third lumbar segments are above the upper level of the second lumbar vertebra. The upper second lumbar and the lower thoracic segments have their roots at a level three vertebrae higher; the upper thoracic and lower cervical segments are two vertebrae higher; and the upper cervical segments, one vertebra higher. The first cervical roots emerge between the skull and the atlas. By carefully studying the sensory, motor, and visceral changes, the segment which is involved in disease or injury may be identified. In addition to symptoms and signs referable to the segment involved, changes due to the interruption of the long tracts aid in the proper diagnosis of the level of the lesion.

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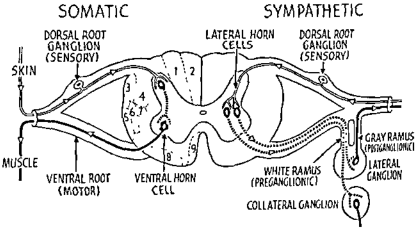

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anoxia (from anesthetic reaching too high a level and causing paralyses of diaphragm, or intercostal muscles; the drop in blood pressure plus loss of blood during operation; mechanical difficulties due to pressure on the diaphragm, etc.), and lastly, thrombosis and embolism due to hypotension and stasis from leg inactivity. Spinal anesthesia has a definite and useful place in surgery because of the good relaxation that is obtained.

Injuries to the cord may be produced by fractures, dislocations, and fracture dislocations of the vertebra (see Chapter 21), penetrating and perforating wounds, severe jarring with resultant hemorrhage. Rarely hemorrhage occurs without injury as in hypertension and arteriosclerosis.

As in injury to the head, it is impossible to tell the degree of cord damage by the extent of vertebra trauma. The spinal cord is subject to the same degrees of injuries as the brain; namely, (1) concussion, (2) edema, (3) contusion or bruising, (4) laceration (incomplete or complete), (5) hemorrhage, hematomyelia (bleeding within the cord), and hematorachis (bleeding outside the cord with pressure on it). Also as in brain injuries these changes are rarely encountered singly and therefore in most instances there is some edema and hemorrhage with lacerations or penetrations, etc.

Nerve cells and nerve fibers (no neurilemma) in the cord are incapable of regeneration if destroyed. *Concussion* produces a complete functional block due to cell alterations principally in interneurons consisting of chromatolysis. Long ascending and descending fiber tracts are involved. The effects are transient.

Edema and some degree of hemorrhage may accompany any injury to the cord and may produce temporary functional impairment by compression. Therefore in examining a patient who has been injured any remnant of function gives hope that nerve cells and fibers have not been destroyed by laceration or severe contusion. Compression by localized accumulation of blood clot or by fracture dislocation may produce symptoms requiring surgical intervention.

Clinical Manifestations of Cord Injury

The history of the accident and points of injury often give a clue as to the level and degree of injury. If in transit there is some motion of the upper extremities and none of the lower, the level may be suspected. Cervical injuries may interfere with respiration. If, in addition, the legs are moved ever so little, there is hope of a functional impairment rather than complete destruction. Examination must be painstaking and thorough, remembering always that associated injuries of the skull, thorax, abdomen, and extremities may be present. Penetrating and perforating injuries may be definitely located, but the extent of internal damage is determined by symptoms and signs.

The motor function, sensory function (light touch, pain sense, heat, and cold), reflexes, and visceral functions are carefully observed. Bedside x-ray examinations are also made to help in the diagnosis.

Complete transection of the cord may produce three stages; namely, (1) spinal shock with complete loss of visceral and somatic sensations and flaccid paralysis; may last two to three weeks; (2) stage of reflex activity with paraplegia in flexion; may be entirely absent; (3) failure of all reflex activity (Bastian's rule).

Autonomic changes are chiefly visceral but may produce pallor or redness (angiomotor), with or without sweating (sudomotor). Sphincteric control of the bladder and rectum may be interfered with. By carefully testing zones of the body for these changes, and by tracing the zones back to the spinal segments, the lesion may be located. Manometric readings may be helpful. A lumbar puncture is made and a water manometer (Becton-Dickinson, # 5027) attached. The initial pressure is recorded (normal, 60 to 180 mm.). With each pulsation there is a 2 to 5 mm. variation and with respiration, 4 to 10 mm. If there is no obstruction in the subarachnoid space (tumor adhesive arachnoiditis, compression from outside dura), pressure will rise on straining or coughing. If a block exists, no change occurs. *Queckenstedt's* test consists of compressing the neck veins for ten seconds. This results in a rise in pressure 150 to 300 mm. and ten seconds after release there is a fall to normal. If a block is present, the rise is delayed or incomplete. Partial blocks cannot be detected by this method unless there is combined lobar and cisternal puncture. In addition, opaque media are sometimes injected into the cisterna magna or lumbar puncture and traced with the x-ray, although intrathecal injection of iodized oil is followed in over 50 per cent of the cases by fever, headache and aggravation of previous symptoms. The oil is very poorly absorbed and some patients have definite, permanent clinical ill effects due to arachnoiditis or encysted accumulations.

Diseases and Injuries of the Spinal Cord

Congenital anomalies of the spinal column and cord are discussed in Chapter 21.

Functional alterations in the cord or its nerve trunks may be purposefully produced by the injection of anesthetic agents. The following methods are employed: (1) Local field block—injection of anesthetic agent into the skin or mucous membrane; (2) nerve block—intraneural or paraneural injections of nerve trunks; (3) paravertebral block—injection of spinal nerves at their points of exit from the spine; (4) plexus block—injection of anesthetic into the cervical, brachial, or lumbosacral nerve trunks; (5) splanchnic block—injection of anesthetic agent into the prevertebral tissues reaching the splanchnics and celiac plexus; (6) caudal block or epidural block—use of anesthetic agents in the sacral canal to anesthetize the terminal trunks of the cauda equina; (7) spinal anesthesia—the introduction of anesthetic agents into the subdural space with quick absorption by the nerve roots blocking the passage of sensory motor and sympathetic impulses.

Spinal anesthesia produces a fall in blood pressure as a result of vasodilation. To limit this effect, some advocate the Trendelenburg position so that blood can reach the brain and vital centers and heart. At the same time this position favors the upward flow of the agent (if its specific gravity is heavier than the spinal fluid), causing more widespread vasodilation. Ephedrine or Adrenalin must be available to relieve this effect. Usually the Fowler position is used to hold the anesthetic agent at a low level. *Complications* of this type of anesthesia include paresthesias, bladder difficulties, convulsions, meningitis, coma due to

anoxia (from anesthetic reaching too high a level and causing paralyses of diaphragm, or intercostal muscles; the drop in blood pressure plus loss of blood during operation; mechanical difficulties due to pressure on the diaphragm, etc.), and lastly, thrombosis and embolism due to hypotension and stasis from leg inactivity. Spinal anesthesia has a definite and useful place in surgery because of the good relaxation that is obtained.

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Complications and sequelae of cord injuries include the paraplegic state, disordered urinary bladder function, the occurrence of root pains or visceral or diffuse burning pains, dysfunctions of the autonomic nervous system, decubitus ulcers, urinary calculi, bowel dysfunction, and psychological and emotional disturbances.

The bladder dysfunction is a major problem, since it occurs with lesions anywhere in the cord—the more complete, the closer the injury, so that destruction of the sacral cord completely denervates the bladder. Although the bladder becomes atonic at first, later it may become autonomous, actually undergoing hypertrophy if residual is kept down by catheter drainage and infection forestalled by this drainage plus chemotherapy and antibiotics. Automatic micturition finally develops—earlier and with greater efficiency in lesions between the seventh cervical and fifth thoracic. It does not appear in the presence of incomplete cord lesions. It is less apt to occur early in lesions below the tenth thoracic. Of course if there are bladder neck obstructions, bladder sepsis, multiple calculi, or severe debilitation, the bladder will not become automatic, and cystotomy may be necessary.

Paraplegia is the inevitable result of severe cord injury, rendering the patient helpless, and if not properly supervised and treated, many complications may occur; namely, malnutrition, decubitus ulcers, injuries to the paralyzed extremities with poor healing (due chiefly to inactivity, venous stasis, and hypoproteinemia), urinary infection, and mental depression. In addition, there may be severe pain which may be of three types, alone or in combination: (1) Somatic pain which is sharp and intermittent and conforms to dermatome patterns, especially those in which no sensation is present. It is seen frequently in injuries of the cauda equina and corresponds to the "phantom pain" previously discussed. Hyperalgesia of the segments directly over the site of injury may amount to pain. (2) Sympathetic pain is constant, dull, aching, or burning and is referred to the back of the leg. This includes so-called visceral pain. (3) Psychic pain which has no definite pattern.

Treatment depends upon causative factors but in all types and particularly those due to vertebral fracture or fracture dislocation the patient must be handled with extensive care and the spine carefully supported. After the patient enters the hospital, a careful examination is made, including bedside x-ray. The examiner looks for associated injuries, evaluates blood loss and anoxemia, and institutes treatment along all lines, but the relief of anoxia and arrest of hemorrhage take precedence over all other problems. Then gastrointestinal or other visceral disruptions must be closed.

Pressure on the cord, like cerebral compression, is usually treated conservatively. If the cord has been hopelessly lacerated, surgery does no good and, if not, laminectomy may jeopardize the life of the patient and at the same time may actually add to the cord injury. If edema or

hemorrhage is the cause, cautious observation is best because the former will be absorbed and the latter may be. Therefore immobilization of the spine in a plaster jacket is indicated. In cervical fractures head traction is indicated and is obtained by calipers or tongs or by a special metal bar included in the head cast. The patient is placed in a special bed with an incorporated Bradford frame arrangement to permit turning and use of the bedpan.

Surgery (laminectomy) is instituted to relieve persistent subarachnoid block due to hemorrhage or foreign bodies. This may be determined by symptoms and signs and lumbar puncture. Penetrating wounds of the spine were treated by prompt exploration during World War II.

The *bladder* requires meticulous care until automatic emptying occurs. At first there will be constant dribbling due to distention and overflow and this predisposes to bladder infection as well as decubitus ulcers. An indwelling catheter is anchored and irrigated with weak potassium permanganate. Antibiotics may be necessary. Manometric readings show the progress of response of the bladder to sensory stimuli, from the bladder itself, the region of the external genitals by way of the sacral cord segments below the injured area, or by other pathways previously discussed. (See Chapter 23.)

The bowel also requires much care and usually does not become automatic as readily as the bladder. Enemas are used after the morning or evening meal to encourage regular bowel emptying.

Good nursing care is required to prevent decubitus ulcer and injury to the insensitive areas. Early ambulation is desired and may be helped by reconstructive orthopedic procedures to provide stabilization of joints and return to motion. Rehabilitation includes corrective exercises, special training in the use of braces, crutches, traction, and special sliding and walking devices to enable the patient to handle himself and to earn a living. Pain may be relieved by sympathetic nerve block, procaine hydrochloride injection in "trigger zones," caudal or spinal anesthesia as a trial for surgical procedures: sympathectomy, decompressive laminectomy having dura open, dorsal rhizotomy (section of posterior roots at certain levels), and chordotomy (section of anterolateral spinothalamic tracts).

Hematomyelia or diffuse hemorrhage into the cord not due to injury is treated by bed rest and prevention of decubitus ulcers. Early ambulation is desirable. Spinal apoplexy belongs in this group.

Inflammations may occur outside the dura in the epidural space, in the meninges, or in the cord itself. The *epidural* space is dorsal to the spinal roots; there is no space anteriorly where the dura is firmly adherent to the vertebrae. There is a potential space in the cervical region and a variable one from the seventh thoracic to the second sacral where the space ends. It is widest at the ninth to eleventh thoracic and third and fourth lumbar. It is filled with fat, blood vessels, and loose areolar tissue. An abscess may form in this space from a pyemia (furuncles,

middle ear disease), from vertebral osteomyelitis, or from injury and direct infection. The disease is rare and is recognized by the history of boils or injury, fever, root pains, and weakness in the legs. Treatment consists of prompt relief of pressure by laminectomy well above and below the involved area and drainage. The dura is not opened. Penicillin should be used.

As a result of delayed softening of a vertebra following a compression fracture (Kümmell's disease) or tuberculous infection with necrosis (Pott's disease), the cord is compressed due to angulation of the vertebral column, passive congestion, and thickening of the dura. Treatment is directed to stabilization of the vertebral column by cast or fusion.

The Meninges

The dura may be irritated by contiguous infection (pachymeningitis) originating in the vertebral bodies or by an open wound or rarely following laminectomy. Tuberculosis and syphilis may also cause inflammation of the dura alone. In all such cases the clinical manifestations may suggest meningitis. However, the spinal cord is free of cells and globulin though under increased pressure.

Leptomeningitis may be caused by the meningococcus, the tubercle bacillus, and the spirocheta pallida. The infection may reach the meninges by the blood or lymph stream, by trauma, or by extension from neighboring structures. The diagnosis is made by the symptoms and signs: headache, malaise, irritability, restlessness, delirium, coma. Vomiting is often present. Convulsions, root pains, and paralysis are common. Stiffness of the neck (Kernig's sign) is characteristic but is not always present and the reflexes may be normal. The spinal fluid is turbid, filled with polymorphonuclears (acute type). A pellicle may form in the tuberculous type. The treatment for the acute variety consists of large doses of penicillin and sulfadiazine. The tuberculous type is helped by streptomycin and the syphilitic variety by penicillin and antisyphilitic therapy. The spinal medulla may be inflamed (myelitis). The causes are (1) infection, which may be primary (poliomyelitis) or secondary (postvaccinal meningitis, by lymphatic extension from kidney, bladder, or pelvic viscera, direct extension from empyema; embolism in septicemia and endocarditis); (2) toxins, carbon monoxide, chloroform, spinal anesthetics, alcohol injections, cachetic and anemic states, pregnancy; (3) trauma, direct or indirect injury (electric shock), penetrating and perforating wounds. The symptoms and signs include motor, sensory, reflex, visceral, and trophic disturbances. The diagnosis is made by the history, symptoms, and signs and study of the spinal fluid. There is a chronic type of myelitis which evolves slowing, causing weakness, heaviness, and stiffness of the extremities and paresthesias. Treatment depends upon the cause, and except for the compression types associated with injury or disease of the vertebrae, surgery is not indicated. The

diagnosis is difficult to make because of the similarity of the symptoms in cord tumors, vertebral disease, combined sclerosis, *multiple sclerosis*, myelomalacia and pachymeningitis.

Neoplasms of Spinal Cord

Neoplasms of the spinal cord produce alterations in sensation and motor function in the extremities, pain which is usually worse at night and is a constant radicular pain, impairment of bladder function which is progressive as well as sexual impotence in the male. The diagnosis is made by careful general and neurological examination, x-ray of the spine, lumbar puncture with study of spinal fluid, Queckenstedt test, and myelography with radiopaque substances. Fifty per cent of the tumors affecting the spinal cord are amenable to surgery. The earlier the diagnosis the less chance for irreparable cord damage.

Types of Tumors

Extramedullary tumors produce sensory changes in the distal parts of the extremities and saddle area and radicular pain which is severe and persistent; they usually do not involve the sphincters. Sometimes these growths contain calcium or alter the size of the interpedicular space, giving rise to x-ray evidence of their location. They consist of: *Meningioma*, which is encapsulated, grows from the dentate ligament, and may project on either or both sides of the vertebrae. It can be completely removed, although the nerve root may be injured in the process. *Perineural fibroblastoma* which requires the sacrifice of the nerve root for its removal. It may be associated with multiple cord tumors (von Recklinghausen's disease) and occasionally gliomas. In multiple neurofibromas only those causing symptoms are removed.

Gliomas may be primary or secondary to brain gliomas. They include: *Medulloblastoma* (usually secondary). *Ependymoma*, the most common primary spinal glioma. It arises in conjunction with the filum terminale and the central canal and may be cystic. Removal is difficult, especially when the cauda is extensively involved. Decompression relieves pain, and x-ray therapy may influence the rate of growth favorably. *Astrocytomas* and *glioblastomas multiforme* are usually not removable. *Angioma* is usually of the cavernous type and occurs at any age. It is usually diagnosed by its position (cervical and thoracic region) and x-ray studies with myelography.

Epidermoid cysts are seen in the caudal region with increasing pressure on the cauda equina. The same is true of neurenteric cysts. They are often completely removable.

Tumors of the vertebra which may exert pressure on the cord or invade it include Hodgkin's disease, lymphosarcoma, metastatic neoplasms (carcinoma of prostate, breast, and hypernephroma, etc.), neurofibromas and perineural fibromas of the posterior mediastinum (hour

glass tumors, Chapter 19) and elsewhere along the cord, tuberculoma, and protruding intervertebral disc (lumbar usually, sometimes cervical). Treatment depends on the cause. Neurofibromas and degenerated nucleus pulposus may be completely removed. Lymphoblastomas respond to x-ray therapy as a rule.

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Chapter 19

The Respiratory System

EMBRYOLOGY AND HISTOLOGY

In the early embryo, when the head and tail folds develop, blind entodermal tubes are formed, both cranially and caudally from the vitelline sac. These are known as the foregut and hindgut, respectively. The foregut later forms part of the oral cavity and is further differentiated into the pharynx and its derivations into the esophagus, respiratory organs, stomach, and duodenum. In 2½ mm. embryos, the respiratory organs appear as a groove in the floor of the entodermal tube caudal to the pharyngeal pouches. On the outside of the tube this groove produces a ridge which becomes larger and rounded at its caudal end. This laryngeal tracheal groove and the ridge develop into the larynx and trachea. The rounded end is the forerunner of the lung.

Externally, two lateral longitudinal grooves mark off the posterior esophagus from the anterior respiratory anlage. The lung bud increases in size and becomes bilobed in 4 to 5 mm. embryos. The lateral furrows become deeper and separate the lung anlages and the tracheal tube from the esophagus. Sometimes the upper part of the esophagus ends blindly and the lower portion opens into the posterior portion of the trachea just above the bifurcation, forming a tracheoesophageal fistula at birth. These anomalies are discussed in Chapter 20. Soon the lung bud extends caudally and divides into two branches, forming the two main bronchi, which divide repeatedly and become separated by a mass of dense entodermal or mesenchymal tissue. It is not definitely known which type prevails. This tissue has a glandlike structure and later unites with the alveolar ducts. It is thought by some that a failure of this union is responsible for congenital cystic disease of the lung.

The primitive bronchi are lined with cuboidal epithelium. They branch dichotomously and are completed by end buds lined with cylindrical epithelium. In the 3- to 4 month stage, many blood vessels appear within this tissue and there is an increase in connective tisue. Also, large lymphatics, which seem to divide the pulmonary tissue into lobules, make their appearance. At 6 to 7 months, the bronchi are lined in part with ciliated epithelium which flattens toward the peripheral ends of the bronchi. These bronchi branch and end in the terminal ducts capped with end knobs. The latter finally become the alveoli. The cuboidal entodermal cells lining the alveoli become interrupted by blood vessels penetrating them and their exact fate is unknown (Bloom). The lung does not increase in size by distention of existing ducts and alveoli, for it has been shown by actual count that there are many more alveoli in the adult than in the newborn.

The trachea divides into two main stem bronchi and these divide into ten smaller bronchi on each side, although their distribution varies. These give rise to still smaller bronchi, from which fifty to eighty bronchioles originate in each lobule. Terminal bronchioles continue into one or more respiratory bronchioles. These divide into two to eleven alveolar ducts from which arise the alveolar sacs or alveoli. Accompanying the bronchi are the pulmonary veins and arteries, forming a surgical unit but not strictly a bronchovascular unit because of intersegmental distribution.

The trachea is lined with ciliated pseudostratified columnar epithelium. It is often referred to as respiratory epithelium. Many elastic fibers, glands, and an incomplete ring of hyaline cartilage (posteriorly there is none) surround the trachea and make up its wall. The bronchi are lined with the same type of epithelium. They have much elastic tissue and smooth muscle. The latter is more plentiful in the

bronchioles and continues into the alveolar ducts. This myoelastic layer is important in connection with the physiology of respiration as it provides the elastic recoil of the lung. The cartilage gradually disappears in bronchioles of 1 mm. The respiratory bronchioles are lined with ciliated columnar epithelium in their proximal parts, and in their distal extremities this becomes low cuboidal without cilia. Some alveoli bud off here opposite the side along which the pulmonary artery runs. These are the first alveoli and, therefore, these tubes have been called respiratory bronchioles.

The alveolar ducts contain strands of elastic and collagenous fibers and smooth cells. Their lining is probably made up of flattened epithelium. The space between the alveolar ducts and sacs is called the atrium. This space is surrounded by collagenous fibers. The alveoli are polyhedral formations, one side of which is always lacking, so that air may get in. There are many capillaries in the alveolar walls and they anastomose freely. Reticular and elastic fibers form the supporting framework for the air vesicles and the capillaries. The elastic and collagenous fibers around the alveoli and ducts are connected with the collagenous fibers in the walls of the arteries, veins, and bronchioles.

There is much dispute concerning a lining of the alveoli. The cells which are present are thought to be endothelial cells making up the walls of the capillaries. The cells outside the capillaries may be connective tissue or epithelial, but they have the appearance and functions of macrophages. These are called septal cells. It would seem that many alveoli are composed merely of capillary loops without any lining at all, or at best a discontinuous membrane with capillaries uncovered and surrounded by a small amount of fluid (lymph).

Histologists have long maintained that alveolar apertures exist permitting collateral ventilation to occur when differences in pressure arise between contiguous lobuli during respiration. Thus the component parts of a pulmonary lobe have communications between them as described by van Allen and co-workers and more recently by Baarsma and Dirkin and van Allen and Lindskog. The existence of anastomoses between the finer ramifications of bronchi has not been proved.

Clinical observations have confirmed the morphological studies which show the existence of interalveolar communications. Upon obstruction of a bronchus, atelectasis occurs only when access of air to an entire lobe has been prevented. If the obstruction affects only part of a lobe, no atelectasis occurs. Thus air must get in around the obstruction. However, inflammation in the obstructed parts prevents the collateral ingress of air and causes atelectasis.

Experimental studies by van Allen and Jung confirmed the morphological studies and clinical observations of collateral ventilation. They introduced a catheter which obstructed the lower lobe bronchus *just past the first bifurcation*. The free end of the catheter was kept under water. At every inspiration water was sucked up into the catheter about 5 cm., and with every expiration air bubbled out as long as the experiment lasted. If now the catheter was introduced so that the obstruction in the bronchus was placed before the first bifurcation and so that the entire lobe could only ventilate through the catheter, air escaped from the immersed end only once. This proved that a collateral access of air outside the obstructed bronchus is possible provided there is free communication of a part of the lobe with the air outside. Moreover, the recent work of Baarsma and Dirkin shows that such communications are not the result of ruptured alveoli.

The collateral air drifts fill in the alveoli distal to obliterated bronchi, thereby avoiding dead space. The ''leafless limb'' is, in reality, an obliterated bronchus with alveoli filled with air from adjacent lung. Bronchiectasis may start as an obliterative bronchiolitis with fibrosis, and the element of inflammation prevents collateral air drifts from functioning so that areas of atelectasis are present.

Frequently the alveoli in the fetus are epithelialized but this epithelialization disappears before birth. Rarely this epithelialization is seen at birth. Such children do

not usually survive. Their lung alveoli show definite epithelial layers and capillary loops between the epithelialized septa.

The reasons for discussing the various types of cells which make up the lining of the lung tubes and sacs are, first, to be able to better understand the physiology of respiration and, second, to understand the various types of lung neoplasm which may be as variable as the cells found in this system.

Anatomy

The pulmonary artery, pulmonary veins, and bronchi are subject to great variations. The same must necessarily be true of the lung segments which constitute the "lung units." Angiocardiographic studies help to define the normal and recent cadaver dissections have added to the knowledge of aberrancies or variations.

The pulmonary artery arises from the conus arteriosus at the pulmonary semilunar valves to the left of the ascending aorta and then ascends to a point below the aortic arch where it gives off the left and right main branches. The *right branch* lies posterior to the ascending aorta and the superior vena cava and anterior to the bifurcation of the trachea, the esophagus, and thoracic duct. In the lung it divides into superior and inferior branches. The *left branch* lies in front of the left main bronchus and descending aorta and below the descending aortic arch of the aorta, to which it is connected by the ligamentum arteriosum, and above the pulmonary veins. The right main branch as seen by angiocardiography averages about 23 mm.; the pulmonary trunk, 26 mm.; and the conus 19 mm. Aneurysms of the pulmonary artery have been described.

The terminal pulmonary veins, two on each side, open into the left atrium of the heart. Then tributaries arise in capillary plexuses in the walls of pulmonary alveoli.* Smaller veins unite to form larger ones, which run along the anterior aspects of the bronchial tubes. The bronchi, arteries, and veins form *segments* within the lobes. Between the segments there exist communications between veins known as "intersegmental veins." They constitute a landmark for the dissection of segments during surgery which should be briefly described. First the segmental artery and bronchus are identified as described by Overholt and Langer and divided. Any subpleural veins and the segmental veins are divided. The lung is then inflated and the distal end of the divided branches grasped. Close inspection reveals one or more veins not following the branches which border the segment being retracted. By carefully following this distally, dividing the small veins which go from the diseased to the healthy segment, the surgeon will find the areolar tissue between segments. The terminal pulmonary veins are in relation with the following structures at the hilus: the upper pulmonary veins on each side lie below and in front of the pulmonary artery. The lower veins are in the lowest part of the root, in a plane slightly posterior to the upper. On the right side the upper vein passes behind the superior vena cava and the lower behind the right atrium close to the interatrial septum. On the left side both upper and lower pulmonary veins cross anterior to the descending aorta and they terminate in the upper and posterior part of the left atrium near its left border. All four pulmonary veins perforate the fibrous layer of the pericardium and receive partial coverings of the serous layer before they enter the atrium.

THE CHEST WALL

The thoracic wall forms a bony cartilaginous and muscular cage, anchored in front to the sternum and behind to the vertebrae. The muscles attached to the first rib, the clavicle, and the scapula on each side form what might be called the roof, and the diaphragm, the floor. The intercostal muscles fill in the spaces between the ribs; and the latissimus dorsi, the serratus anterior, the shoulder muscles, and the erector spinae group cover the posterior and the lateral surface of the chest, the pectoral muscles cover the upper anterior surface, while the rectus abdominis is attached to the lower anterior

surface. The opening of the thorax at the top is small. It lies between the manubrium sterni, in front, and the vertebral column, behind. Through it pass the great vessels (the carotid arteries and the subclavian and internal jugular veins), the vagus nerves, the trachea, and the esophagus. Small openings in the diaphragm permit the esophagus to join the stomach and allow the abdominal aorta to emerge and the inferior vena cava to enter. The blood supply of the thoracic wall is chiefly through the intercostal arteries, which come from the thoracic aorta and (together with the intercostal nerves) run along a groove on the inferior margin of each rib. In addition, the important internal mammary arteries run along the lateral aspect of the sternum to join the superior epigastric artery, whereas behind, the vertebral arteries follow the course of the spine. The nerves which control the movements of the thorax are the intercostal nerves, the long thoracic nerve to the serratus anterior, the thoracodorsal nerve to the latissimus dorsi, and the phrenic nerve which runs inside the chest to the diaphragm. These nerves supply the impulses necessary for breathing. Since the ribs slant downward, their elevation increases the anteroposterior diameter of the chest. During the act of inspiration the ribs are elevated and the diaphragm descends; the negative pressure thus created together with the elasticity of the lung permits inhalation to occur. This is the active phase. Then the ribs fall downward, the diaphragm ascends to its normal position, and the lung, due to its elastic recoil, contracts, thus allowing expiration to take place. Within the chest wall are the pleura, the lungs, and the mediastinum, with its vital contents; namely, the heart and the great vessels.

THE PLEURA

The pleura is a thin sheet of mesothelium made up of a single layer of cells. It is folded upon itself, forming two layers: a parietal layer, which lines the inside of the thorax, and a visceral layer, which is firmly attached to the outside of the lung. The folding occurs at the root of the lung, but the pleura is everywhere continuous, forming an airtight cavity. Since the pleural cavity is larger than the lung, a pleural space exists, which is important in respiration. The pressure in the pleural cavity is normally always negative; that is, lower than atmospheric pressure. It is more negative with inspiration and less negative with expiration, and this change, as we have seen, is due to changes in the position of the chest wall and diaphragm. Normally we breathe both with our thorax (thoracic breathing) and with our diaphragm (diaphragmatic breathing); however, we can breathe with one or the other, if necessary. It is easily seen that when the pleural space is increased, a greater degree of negative pressure results, creating a partial vacuum and thereby pulling the elastic lung out. This is an active process and differs from expiration, which is passive and consists of a decrease in the size of the pleural space, permitting the elastic lung to recoil. If, however, the intrathoracic pressure is positive, as a result of air entering through a rupture or wound of the pleura or lungs, then the lung immediately collapses. If this occurs on one side, a dangerous mediastinal shift may occur, but life is usually preserved; if on both sides, death from asphyxia may result. This process is slightly different in children and will be discussed later under empyema.

The blood pressure in veins is much lower than in arteries (see Chapter 17), being highest in peripheral veins and lowest in the vena cavae as they enter the right auricle. At this point the pressure is negative, thereby permitting the blood to find its way back to the heart through the valveless veins of the abdomen and thorax. *But the blood pressure in the large veins, though low, is higher than the pressure in the thoracic cavity, else the flow of blood would be interrupted. Thus, any lesion which increases the intrathoracic pressure will cause passive congestion in the veins, causing the large veins of the neck to stand out. Also,* there will be a dangerous dilatation of the right side of the heart because of its effort to pump the blood through collapsed ... the left ventricle will beat rapidly, though weakly, in an attempt to keep the

arterial system supplied. Should this continue, less and less blood, poor in oxygen, will reach the left ventricle. There will be extreme cyanosis due to an increased amount of reduced hemoglobin. The blood pressure will fall rapidly due to cardiac failure. Except in accidents, or erosions of a vessel from disease, pathological changes develop slowly, permitting adjustments to take place.

PHYSIOLOGY OF RESPIRATION

Breathing consists of moving blood (perfusion) and moving air (ventilation) through the lungs. The respiratory center is normally under the control of:

1. Chemical influences. Carbon dioxide is probably the controlling factor; however, lack of oxygen may excite the center also. In Chapter 12 we have seen that the pH of the blood may influence the center. Carbon dioxide excess increases chiefly the depth of breathing.

2. Nervous stimuli.

a. These are carried chiefly by the vagi, which act to offset any changes in respiration. When the lungs are distended with air, afferent vagal impulses inhibit the automatic action of the center and arrest inspiration, thereby bringing on expiration: when the lungs are empty of air, these impulses stop, thereby arresting expiration and permitting inspiration to occur. (Hering-Breuer reflex). Therefore, the vagi influence both the *rate* and *depth* of breathing.

b. Sensory stimuli for any portion of the body carried over sensory nerves may have a *pressor* effect, causing quicker and stronger inspiration, or a *depressor* effect, causing respirations to become slower, or more feeble, or even to cease entirely.

c. Voluntary control may be exerted over respiratory movements.

d. The carotid sinus is influenced by pressure changes (see Chapter 14). The carotid body is stimulated by a low oxygen content of arterial blood or by carbon dioxide content to some extent. As blood pressure rises, the depth of respiration decreases and if this continues, apnea occurs. It is the lack of oxygen and the hydrogen ion concentration which affects the carotid sinus.

The passage of gases is but a process of simple diffusion. The total epithelial surface of the lungs is 70 square meters. Of this, 55 square meters is respiratory; that is, over 25 times the surface area of the skin. The capillaries in the respiratory portions of the lungs have a surface of 140 square meters. The lungs eliminate about 800 c.c. of water per day and may eliminate other substances from the blood, such as alcohol. The body at rest uses only about one-twentieth of areating surface. The alveoli change little during inspiration and the flow of blood is faster then. The alveolar ducts become distended and also the small bronchi and bronchioles providing the area into which air is inspired.

The fetus probably makes some furtive respiratory movements in utero, sucking small amounts of liquor amnii into the lungs. Air gets into the body through the trachea and to some degree by swallowing or sucking, with resultant absorption of oxygen from the gastrointestinal tract. Tissue pressures are everywhere equal to atmospheric pressure except in the thorax and abdominal cavities. At birth, the intrapleural and intrapulmonic pressures are probably equal. This condition would not permit respiration to occur. However, very soon after birth, the pressure within the pleural cavity becomes negative to atmospheric pressure. This is possible because of two conditions: (1) the walls of the pleural cavities are mechanically resistant enough to allow pressure differences to occur. (2) the withdrawal of water and crystalloids from the pleural space permits the lungs to expand by creating the negative pressure. Since the osmotic pressure in the capillaries of the pleura is normally about 360 to 400 mm. of water and since the hydrostatic pressure is not more than a few centimeters of water, therefore water is drawn out of the pleural cavity into the blood, and the lungs are thereby expanded (Krogh). The changes necessary to expand the lungs fully will determine the final pressure reached.

surface. The opening of the thorax at the top is small. It lies between the manubrium sterni, in front, and the vertebral column, behind. Through it pass the great vessels (the carotid arteries and the subclavian and internal jugular veins), the vagus nerves, the trachea, and the esophagus. Small openings in the diaphragm permit the esophagus to join the stomach and allow the abdominal aorta to emerge and the inferior vena cava to enter. The blood supply of the thoracic wall is chiefly through the intercostal arteries, which come from the thoracic aorta and (together with the intercostal nerves) run along a groove on the inferior margin of each rib. In addition, the important internal mammary arteries run along the lateral aspect of the sternum to join the superior epigastric artery, whereas behind, the vertebral arteries follow the course of the spine. The nerves which control the movements of the thorax are the intercostal nerves, the long thoracic nerve to the serratus anterior, the thoracodorsal nerve to the latissimus dorsi, and the phrenic nerve which runs inside the chest to the diaphragm. These nerves supply the impulses necessary for breathing. Since the ribs slant downward, their elevation increases the anteroposterior diameter of the chest. During the act of inspiration the ribs are elevated and the diaphragm descends; the negative pressure thus created together with the elasticity of the lung permits inhalation to occur. *This is the active phase. Then the ribs fall downward, the diaphragm* ascends to its normal position, and the lung, due to its elastic recoil, contracts, thus allowing expiration to take place. Within the chest wall are the pleura, the lungs, and the mediastinum, with its vital contents; namely, the heart and the great vessels.

THE PLEURA

The pleura is a thin sheet of mesothelium made up of a single layer of cells. It is folded upon itself, *forming two layers:* a parietal layer, which lines the inside of the thorax, and a visceral layer, which is firmly attached to the outside of the lung. The folding occurs at the root of the lung, but the pleura is everywhere continuous, forming an airtight cavity. Since the pleural cavity *is larger than the lung,* a pleural space exists, which is important in respiration. The pressure in the pleural cavity is normally always negative; that is, lower than atmospheric pressure. It is more negative with inspiration and less negative with expiration, and this change, as we have *seen,* is due to changes in the position of the chest wall and diaphragm. Normally we breathe both with our thorax (thoracic breathing) and with our diaphragm (diaphragmatic breathing); however, we can breathe with one or the other, if necessary. *It is* easily seen that when the pleural space is increased, a greater degree of negative pressure *results, creating a partial vacuum and thereby* pulling the elastic lung out. This is an active process and differs from expiration, which is passive and consists of a decrease in the size of the pleural space, permitting the elastic lung to recoil. If, however, the intrathoracic pressure is positive, *as a result of* air entering through a rupture or wound of the pleura or lungs, then the lung immediately collapses. If this occurs on one side, a dangerous mediastinal shift may occur, but life is usually preserved; if on both sides, death from asphyxia may result. This *process* is slightly different in children and will be discussed later under empyema.

The blood pressure in veins is much lower than in arteries (see Chapter 17), being highest in peripheral veins and lowest in the vena cavae as they enter the right auricle. At this point the pressure is negative, thereby permitting the blood to find its way back to the heart *through the valveless veins of the* abdomen and thorax. *But the blood pressure in the large veins, though low, is higher than the pressure in the thoracic cavity, else the flow of blood would be interrupted. Thus, any lesion which increases the intrathoracic pressure will cause passive congestion in the veins, causing the large veins of the neck to stand out. Also,* there will be a dangerous dilatation of the right side of the heart because of its effort to pump the blood through collapsed lungs, and the left ventricle will beat rapidly, though weakly, in an *attempt* to keep the

The child is therefore born with a negative intrapleural pressure; that is, negative to atmospheric pressure. At birth, therefore, even though the lungs almost fill the pleural cavities, there is a disproportion between the thoracic cage and the lungs which are therefore filled with air due to its inrush to fill the enlarged space. If nothing further occurred, the lungs would remain expanded unless, of course, the pleura should be punctured. However, with a descent of the diaphragm and enlargement of the anteroposterior diameter of the chest which occurs with the first breath, the thoracic cage becomes too large for the lungs to fill by a simple unfolding of the walls of the air spaces. The elastic tissue of the bronchiole tree, blood vessels, and air sacs is put under stress and is constantly pulling against the stretching force. This pull or recoil is about 4 to 5 mm. of mercury.

Intrapulmonic pressure varies from about -2 mm. of mercury or 758 during the inspiratory phase to a 3 or 4 mm. of mercury or 764 during the expiratory phase of ordinary quiet respiration. With the lungs at rest, the pressure is atmospheric or 760 mm. of mercury.

The intrapleural pressure varies from -6 mm. of mercury during quiet inspiration in the adult to -2½ mm. of mercury during expiration. Therefore, at expiration, the intrapulmonic pressure may be 763 mm. of mercury and the intrapleural 757½ mm. of mercury because the entire process began with an elastic recoil of the lungs at birth of -2 to 3, and in the adult it reaches -4 due to the enlargement of the thoracic cavity. Even after forced expiration, the lung is not totally collapsed and the elastic recoil is still there. However, if great enough, this recoil is lost because the chest is made so small that the intrapleural pressure may be 50 or more (that is, 810 mm. of mercury).

Whether the pleural sac is normally real or apparent is inconsequential because the two layers are continuous throughout, although in diseased states they may not be. Therefore, pressures affecting one layer will affect the other unless adhesions or other abnormalities exist.

Blood goes from the right to the left side of the heart through the pulmonary circuit, and the quantity passing per minute must equal the quantity flowing at the same time through the rest of the body; namely, about 5 liters under basal conditions. The mean arterial pressure in the pulmonary circuit is about one-sixth that of the aorta, or about 18-20 mm. of mercury. In the dog there is a systolic pressure of about

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laries. Although this is slight, nevertheless, it does occur in small amounts, and it is quickly picked up by the lymphatics and carried back to the blood stream. Also, the lymph capillaries pick up particulate matter and since they behave as semipermeable membranes, they are entirely dependent upon the positive pressures within the chest. The capillaries in the thorax have a hydrostatic pressure of about 20 mm. of mercury. The osmotic pressure within the capillaries is approximately the same as elsewhere; namely, 25 to 30 mm. of mercury. As we have seen, the negative pressure within the pleural cavity during an ordinary respiratory cycle varies from a -5 to -10 mm. of mercury in an adult. The pressures within the alveolus will vary between a -2 during inspiration to a +4 during expiration. The sum of the outward pressures, if we may use that term, would be the hydrostatic pressure in the capillary, which is 20, plus the negative pressure in the pleura, which is 10, plus the negative pressure in the alveolus during inspiration, which is 2, a total of 32 mm. of mercury. The sum of the pressures tending to keep fluid within the capillaries would be the osmotic pressure, which is about 30, plus the positive pressure in the alveolus during expiration, which is about 4, a total of 34 mm. of mercury. The effective pressure, therefore, tending to keep fluid from leaving the capillaries is about 2 mm. of mercury. In addition, the lymphatics help to keep the lungs dry. It will be noted that during expiration the negative pressure within the pleural cavity is reduced to -5 and, therefore, the total outward pressure, if we may use the term, is 20 plus 5, making 25, whereas the pressure tending to keep the fluid within the capillaries is 30 plus 4, or 34; in other words, an effective pressure keeping fluids within the capillaries of 9 mm. of mercury. We may look upon the pressure within the alveolus as roughly corresponding to that of the interstitial spaces in other tissues of the body. When there is the slightest leakage of fluid within the alveolus, a cough reflex is initiated which increases the intra-alveolar pressure, thereby greatly reducing the effective pressure outward and increasing the effective osmotic pressure or pull inward. So long as the increased alveolar pressure is delegated to segments of the lung and does not include the entire lung space, this method is very effective in preventing the loss of fluid within the alveolus. However, when the entire lungs are simultaneously laboring under increased intra-alveolar pressure, an acute type of emphysema would be present and this, of course, would give rise to labored breathing and anoxia. This actually occurs sometimes in bronchial asthma. The diagram on the lower right is based upon studies by Drinker and Warren: The Genesis and Resolution of Pulmonary Transudates and Exudates: J. A. M. A. 122: 269, 1943.

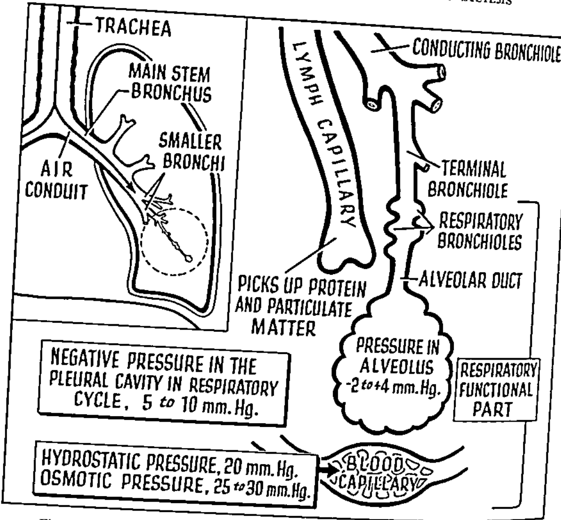

Fig. 211.—Diagram illustrating the physiology of the respiratory functional unit and its relationship to fluid balance. The bronchial tree is divided roughly into two parts. The first part serves merely as an air conduit and apparently has no respiratory function. It consists of the trachea and the bronchi. These divide into ten smaller bronchi on each side, although their distribution varies, as we shall see in subsequent diagrams. These, in turn, give rise to still smaller bronchi from which fifty to eighty bronchioles originate in each lobula. The beginning of the functional unit is probably in the respiratory bronchioles, although the terminal bronchioles may have some respiratory function. The respiratory bronchioles branch into the alveolar ducts and these, in turn, into the atria which communicate with the alveoli.

The pressure within the pleural cavity ranges roughly from -5 to -10 mm. of mercury. They are never positive or the lungs would collapse. During inspiration they will reach a −10, and during expiration a −5 or thereabouts. At the same time, the intrapulmonary pressure will vary from about a -2 mm. of mercury during the inspiratory phase to a +3 or 4 mm. of mercury during the expiratory phase of ordinary quiet respiration. These figures vary greatly. For example· the maximal negative pressure capable of being developed within the lungs by forced inspiration is probably −40 to 50 mm. of mercury; on the other hand, when an expiratory effort is made with the glottis closed, as during coughing or strong muscular effort, the intrapulmonary pressure becomes raised to +10 up 40 mm. of mercury. In the pleural cavity the pressures will also vary greatly, although the normal is between a −2 to −6 mm. of mercury during ordinary respiration. With a strong inspiratory effort with the glottis closed, it may amount to −40 mm. of mercury, and in forced expiration under the same circumstances the entire negative pressure may be abolished and instead a positive pressure up to 50 mm. of mercury may be substituted. With these extremes in mind it will be seen that during inspiration the average negative pressure within the pleural space is about a −6 and during expiration it is about a −2.

The arrangement within the lungs is such that it roughly corresponds to the arrangement in the rest of the tissues of the body insofar as the interchange of fluids is concerned. As in other parts of the body, we have learned in Chapter 11 that the fluid portions of the blood are under two forces as described by Starling. In the lungs the same conditions prevail. The lungs are admirably suited for dryness because it must be obvious that should the alveoli contain fluid, oxygenation would be interfered with. Consequently, in ordinary respiration the lungs remain dry. This is possible because of a prodigious lymph supply which takes care of the protein that might leak from the capil-

(Continued on opposite page)

lieves it is the dyspnea with increased negative pressure of the thorax plus the anoxia which tends to draw fluid out of the capillaries.

The capillaries of the lungs are in a unique position. They get their oxygen from the air and not secondarily from the blood. Therefore, if oxygen is administered therapeutically, it must be given early and under positive pressure.

Lymph capillaries in the lung are constantly picking up protein, and the movement of lymph is greater in moving lungs than in the more quiescent. This is important postoperatively where patients should be urged to take deep breaths.

It is thought by Krogh and Landsberg that protein in pleuritic exudates is gradually broken down by enzymes produced in adjoining cells. The cleavage products are able to diffuse into the blood, and a direct reabsorption of the exudate is made possible.

Due to the negative pressure in the pleura, the lymphatics are usually unable to take up much protein fluid. The positive pressure in the abdomen moves fluid up the lymphatics through the diaphragm into the mediastinum, and, to some extent, into the pleural, lymphatics, and then into the right lymphatic and thoracic ducts.

Exchange of Gases

Atmospheric pressure is 760 mm. of mercury or 14.7 pounds to the square inch. Oxygen pressure in the lungs is 100 mm. of mercury. Ten millimeters of mercury pressure is lost in the capillaries, leaving 90 mm. of mercury in the arteries and a decline to about 30 mm. of mercury in the veins. Only about one-third of the oxygen is given up normally. Sixteen to 24 volumes per cent is the normal capacity in the arteries, a level rarely attained; 0.5 volumes per cent is normal for plasma; and 19 (females) to 20.5 (males) volumes per cent in the hemoglobin. In the veins it is 10 to 14 volumes per cent. The average adult uses about 200 to 250 c.c. of oxygen per minute while at rest.

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Gases expand in the atmosphere in inverse relation to the pressure. One liter of gas at 18,000 feet expands to 2 liters; at 33,700 feet, to 4 liters; and at 42,000 feet, to 6 liters. Since the volume of the chest remains the same, the expanded air contains small amounts of air constituents, and at 42,000 feet there is about one-sixth as much oxygen available as at sea level. Breathing 100 per cent oxygen would do no good because the oxygen molecules will be so diluted that a normal pressure of 100 mm. mercury cannot be maintained. The number of oxygen molecules in a given space become progressively less as the pressure is lowered. Water vapor pressure is constant, but carbon dioxide is lowered by increased breathing as altitude increases. The sum of the carbon dioxide pressure and water vapor pressure must be subtracted from the total to get the oxygen pressure. At a high altitude with a man breathing 100 per cent oxygen, the water vapor pressure may be about 47 and the carbon dioxide about 35 mm. of mercury, a total of 82 mm. of mercury. If the barometric pressure is 138 mm. of mercury, the pressure of oxygen in the lungs would be 56 mm. of mercury at 50,000 feet; alveolar partial pressure is zero.

Altitudes of 3,000 feet or less have no effect on respiration because barometric pressure remains at 760 mm. of mercury up to 5,000 feet, as will be noted from Table XVI.

According to Boyle's law, the volume of gas varies inversely with the pressure, provided the absolute temperature remains constant. This fact is important in entrapped air within the body at high altitudes; also in the anoxic anoxia resulting from low partial pressure within the lungs, as shown above, as well as in the lowered carbon dioxide content due to hyperpnea. The effects of centrifugal force in aviation have been discussed in Chapter 14—Shock, but should be mentioned here as a cause of stagnant anoxemia, "air bends" or "aeroembolism." Air is in the fluids of the body under

40 mm. of mercury and a diastolic pressure of about 10 mm. of mercury and a pulse pressure of 30 mm. of mercury which is higher than the mean pressure. This is the reverse of the systemic pressures. Pressure in the pulmonary veins varies from -3 mm. water in inspiration to +4 mm. of water during expiration. The tone of pulmonary arterioles is low so that a rise on the venous side is transmitted to the arterial side.

Blood pressure in the lungs remains constant even though peripheral pressure rises. However, a rise in aortic pressure is attended by a rise in pulmonary arterial pressure due to a greater amount of blood returned to the right ventricle through the coronary system and not due to back pressure from an inadequate emptying of the left ventricle. The lung has great adaptability and, according to Drinker, a young adult can increase his pulmonary ventilation from a resting volume of 6 liters to 125 liters during exercise. With this change, the cardiac output may rise from 5 liters per minute to 20 liters per minute. With each cardiac systole the lungs receive from the right ventricle as much blood as the left ventricle pumps to the whole body. The lungs possess a blood capacity in terms of instant cardiac output equal to that of the entire body.

The pulmonary circulation is probably not under vasomotor control. The lungs must receive and oxygenate all the blood brought to them. This is accomplished by adjusting the breathing and letting the increased blood flow passively through a capillary bed great enough to carry all the blood that can be sent to it even under the most extreme conditions of cardiac output.

Fluid escaping from the blood capillaries must first be interstitial and, therefore, would result in a thickening of the alveolar partitions which normally, in cross section, contain the blood capillaries and nothing else. If the alveolar wall is deficient, as Josslyn believes, then fluid would go directly into the alveoli. Even the lymphatics do not extend into the alveolar wall past the very beginning of the respiratory portion; that is, the atrium. Any foreign material in the alveolar wall is a barrier to the exchange of gas.

The arrangement in the lungs makes for dryness because the hydrostatic pressure in the capillaries is low, about 20 mm. of mercury. The osmotic is higher, about 25 to 30 mm. of mercury. The pressure in the alveoli is -2 to +3 or 4 and in the pleura -5 to -10 mm. of mercury, an effective outward pressure of about 20 mm. of mercury. The result is an effective osmotic pressure of 5 to 10 mm. of mercury. In addition, the lungs are profusely supplied with lymphatics and lymphoid tissues, both lymphocytes and nodes. By consulting the diagram, it will be apparent that although the hydrostatic pressure of the capillaries plus the negative pressure in the pleural cavity tend to force fluid out, yet the osmotic pressure is so great that the flow is always toward the capillaries.

It is difficult for lymphatics to pick up much in quiet respiration for they behave as a semipermeable membrane and are sensitive to the hydrostatic pressure surrounding them. Their osmotic pressure is very low and therefore perhaps most absorption takes place in expiration when the negative pressure within the pleura is decreased and the positive pressure within the lungs is increased. The same is true during coughing. The right lymphatic duct contains lymph from the heart and lungs on the right side—perhaps some from the lower portion of the left. This duct enters the subclavian vein above the lymph node. The greater part of the left lung supplies lymph to the thoracic duct. Severe respiratory movements, which increase negative pressure in the chest, will produce pleural and pulmonary transudates even if the oxygen is sufficient. If, in addition, there is an anoxia, capillaries will become leaky and edema will easily follow. The lymphatics of the lungs are large and ample and they return the transudates to the blood stream.

In total cardiac decompensation, fluid in the pleural sacs is due to increased pressure in the pulmonary vessels. Drinker believes that the right heart is capable of great dilatation, especially when this occurs gradually, and that leakage due to an increased hydrostatic pressure in the capillaries does not occur for a long time. He be-

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TABLE XVI

VOLUME OF GAS	ALTITUDE IN FEET	BAROMETRIC PRESSURE (MM. OF MERCURY)
1.0	0	760
1.2	5,000	630
1.5	10,000	520
1.9	15,000	430
2.4	20,000	350
3.0	25,000	280
4.0	30,000	230
5.4	35,000	180
7.6	40,000	140
8.8	42,000	130

atmospheric pressure. When atmospheric pressure is suddenly reduced, air will escape from body fluids like carbon dioxide from a carbonated beverage when the cap is removed. This has been termed *decompression emphysema* or "air embolism" and is a counterpart of the disease which is well known as caisson disease seen in men who work down in pressures greater than atmospheric and then suddenly rise to the surface. In either event there is a release of nitrogen from the blood to various tissues, producing pain (the bends), vertigo (the staggers), air hunger (the chokes), and cutaneous manifestations (the itch); in addition, there may be neurological manifestations and paralysis of the bladder and bowels. In each instance the predominating symptom is due to the presence of air emboli which may vary in their location from time to time. Prevention is directed toward gradual ascent, and in aviation breathing oxygen for 2 hours prior to ascent. This results in gradual elimination of nitrogen and the oxygen is used by the tissues and is not released as air bubbles, whereas the nitrogen is present in the tissues at a pressure of about 515 mm. of mercury. Treatment is based on the use of 100 per cent oxygen and recompression in special chambers for caisson disease.

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1.5	10,000	520
1.9	15,000	430
2.4	20,000	350
3.0	25,000	280
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Tests of pulmonary function are designed to reveal the amount of air actually taken in with each respiration or a given period of time, and what is perhaps more important, the absorption of oxygen and release of carbon dioxide. We have seen that *vital capacity* is the amount of air which can be displaced by the lungs during deep inspiration and forced expiration; that is, the sum of complemental, tidal, and reserve air—about 4 to 4½ liters. This can be measured by the *spirometer.* Since this gives the sum of both lungs, it may be advantageous to know how much the normal and the diseased lung contribute to the vital capacity. This may be determined by a special tube inserted under fluoroscopic guidance into the left main bronchus—a *bronchospirometer. Exercise response and maximum breathing capacity* are helpful tests. The former shows dyspnea which may be extreme on exercise in spite of a good vital capacity (emphysema). The latter depends on a series of respirations per unit of time. Some studies made with the bronchospirometer indicate the following normal ranges:

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Asphyxia (from the Greek, *without pulse,* which is appropriate because the rapid weak pulse is one of the earliest signs of asphyxia) means that the lungs are prevented from oxygenating the blood. Smothering,

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cells. Acute cardiac decompensation leads to an anoxic anoxemia due to pulmonary edema and stagnant anoxemia from pooling of much of the blood volume in the veins.

Special Types.—

1. *Aviation or high altitude anoxic anoxemia* is due to the low barometric pressure. This has been discussed previously in this chapter.

2. *Anesthetic anoxemias.* Modern anesthesia begins with sedatives or narcotics administered in the room. These are all respiratory depressants, acting on the center and decreasing the minute volume exchange.

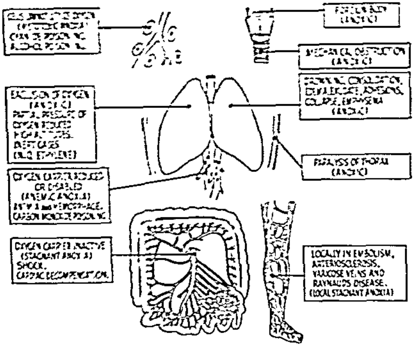

Fig. 212.—Diagram indicating some of the causes of anoxia. The splanchnic area is chosen as an example of stagnant anoxia because of its enormous capillary bed and the frequency of blood pooling in this region.

The great danger of anesthesia in surgery is anoxia. The advantage of one or another type of anesthetic depends a great deal on the ability of the individual anesthetist. Deaths from anesthetics are practically always due to anoxemia. Anoxia must be avoided and is particularly dangerous when it occurs in a patient in the Trendelenburg position (where there is stasis of blood plus a decrease in vital and total capacity of the lungs, thereby leading to stagnant and anoxic anoxemia), or in a patient with paralysis of muscles of respiration or the respiratory center from intracranial lesions or sedatives. There must be no obstruction to breathing. Common causes are: foreign bodies, gum, false teeth, meat, candy, sponges, mucus, vomitus, blood, pus; relaxation of the jaw muscles, permitting the tongue to fall back against the posterior wall of the pharynx; laryngospasm due to local irritation or reflex stimulation; tumors or edema pressing on the respiratory passages; external pressures on

stifling, and *suffocation* mean practically the same thing. *Apnea* means cessation of breathing. *Hyperpnea* is panting or rapid breathing. We use the term *asphyxia* as synonymous with *anoxia* (lack of oxygen) or a deficient supply of oxygen to the tissue cells and *anoxemia* (lack of oxygen in the blood); strictly speaking, the term is a misnomer because a complete lack of oxygen would mean death. A better term would be *hypoxemia* or deficient oxygen in the blood. *Any condition which prevents the tissues from receiving oxygen equal to their needs is spoken of as oxygen want,* oxygen lack, hypoxia, or asphyxia. The body must have oxygen to *live.* If this is absent, or deficient in amount, for even a relatively short time, irreparable damage may occur, due to degenerative changes in the brain, heart, blood vessels, lungs, and intestines.

Causes of Anoxia.—Peters and Van Slyke classify the causes of anoxia as follows:

1. *Anoxic anoxia* (anoxemia) is the reduction in tension of oxygen in the arterial blood and may be caused by:

a. An interference with the passage of oxygen from the air into the blood in the lungs, due to mechanical obstruction, a foreign body in the larynx, drowning, weak respiratory movements, edema, exudates, consolidation, adhesions, collapse, or emphysema.

b. Reduction of partial pressure of oxygen in the inspired air due to inhalation of inert gases, such as nitrogen, hydrogen, nitrous oxide, ethylene, etc.; inhalation of air under reduced (barometric) pressure, as at high altitudes.

c. Inability to use the thorax, as in poliomyelitis.

2. *Anemic anoxia* is the reduction of the oxygen that can be furnished the tissues by the blood. This results when the amount of hemoglobin is decreased, as in anemia or hemorrhage, or when the ability of the hemoglobin to yield oxygen is decreased, as in carbon monoxide poisoning.

3. *Stagnant anoxia* is due to interference with the circulation. The amount of oxygen in the blood is sufficient, but it does not circulate fast enough to supply the tissues, as in shock, hemorrhage, cardiac weakness, or abnormally high venous pressure, as in cardiac decompensation. It may be local, due to a circulatory disturbance, as in spasm of arteries, Raynaud's disease, embolism, arteriosclerosis, varicose veins, etc.

4. *Histotoxic anoxia* is caused by the inability of the cells to utilize the oxygen, even if present. This is seen in cyanide poisoning, alcohol poisoning, and after narcotics.

This classification is basic and inclusive. However, in surgical practice we encounter many *combined* types of anoxemia and some special types whose causes should be considered.

Combined Types.—By this is meant forms of anoxemia due to more than one cause, acting simultaneously. For example, in peritonitis, anoxemia may be classified as stagnant due to pooling of blood in the splanchnic bed, anoxic due to distention and therefore interference with breathing, and anemic due to the effects of the infection on the red blood

anoxemia. This has been known to physiologists for years. The principal effect of asphyxia is on the cell wall which becomes more permeable, disturbing osmotic equilibrium and the interchange of colloids and crystalloids. Different cells are more or less resistant, but the ultimate effect, whether it is in the nerve or endothelial or heart muscle cell, is an effect on the cell wall. Therefore, the similar effects of burn shock, histamine shock, epinephrine, poisoning by nicotine, digitalis, glucosides, parathyroid, carbon disulfide, carbon monoxide, cyanide, nitrites, mercury, lead, and pitressin, to mention only a few, must be interpreted as due to anoxemia—because the same effects, degeneration, necrosis and fibrosis of the myocardium, necrosis and cyst formation in the media of the ascending aorta, as well as changes in the brain, testes, and bone marrow have been observed in all of the above cases.

Recently experiments on aortic anastomosis have reaffirmed the sensitivity of nerve cells to anoxemia (Chapter 17). Reflexes may be abolished in a few seconds and coma may occur in six to eight seconds. Actual permanent damage follows within eight to ten minutes or less. Brain centers survive from twenty to thirty minutes and spinal centers forty to sixty minutes, although we have observed hind leg paralysis in dogs after 18 minutes. These effects are due to an increase in intercellular and intracellular fluid or both. A rise in carbon dioxide tension causes engorgement of the cerebral vascular tree. Blood vessels dilate when carbon dioxide is increased or oxygen reduced. Some observers believe that the so-called "second" wind of the runner is due to a more rapid flow of blood through the respiratory center, relieving the acid condition of the nerve cells. The brain actually increases in size in anoxemia.

The heart is next most sensitive to oxygen lack. At first there is a slowing of the heart rate. However, an increase in pulse rate is one of the earliest signs. This is due to the fact that heart muscle needs about five times as much oxygen as skeletal muscle, which may be deprived for an hour and a half and survive. *Chronic pulmonary disease* is the principal cause of *cor pulmonale*. It is seen in chronic obstructive emphysema, chronic pulmonary fibrosis, silicosis, bronchiectasis, tuberculosis, bronchial asthma, kyphoscoliosis, or primary sclerosis of the pulmonary artery (Ayerza's disease).

Blood vessels are also very sensitive to anoxemia. Capillaries dilate and become permeable. Capillary stasis resulting from oxygen deficiency is irreversible after about fifteen minutes (Krogh).

The lungs show the effects of anoxemia by an increased rate and amplitude of respiration. This hyperpnea reduces alveolar and arterial carbon dioxide tension and results in an increased affinity for oxygen. At the same time there is a rise in blood pressure and pulse rate. Soon there is apnea with cyanosis and if anoxemia continues, death ensues.

Nausea, vomiting, diarrhea, and distention result from the anoxic effects on the gastrointestinal tract. The liver is very resistant to anox-

the neck or chest, especially in infants. Such simple measures as holding the chin up, introducing rubber airway tubes, endotracheal anesthesia, removing bronchial mucus plugs by aspiration or bronchoscopy, limiting excessive bronchial secretions by the use of atropine, slow induction, with ample oxygen, are all designed to avoid states of anoxia. *Perhaps the best anesthetic, especially for the novice, is ether.* If there are any signs or symptoms of anoxemia, the anesthetic should be stopped long enough to determine the cause (therefore the desirability of inhalation anesthetics), and, if necessary, the operation should be interrupted as quickly as possible. Usually acarbia is the cause and this is controlled by the administration of carbon dioxide and oxygen. However, in long thoracic operations the removal of carbon dioxide from the lung is perhaps as important as the administration of oxygen.

Because of the effects of anoxia, "gas" anesthetics are under careful scrutiny at present. Nitrous oxide produces anesthesia really by a continual series of anoxic anoxias alternated with resuscitations by oxygen, although it is said to have some anesthetic properties; therefore, brain complications may occur, especially in the aged and debilitated, where it was formerly thought to be indicated. If anoxemia is present, nitrous oxide would increase it by further reducing the oxygen in the hemoglobin. If there has been a severe hemorrhage, the gas is a poor anesthetic because there is an insufficient amount of red blood cells to transport the gas. More important, if the hemoglobin is below 5 Gm., anoxemia may be present without cyanosis. Ethylene and cyclopropane are also under close observation on the same ground and also because of the liver damage which has been observed to follow cyclopropane. These agents may be given with 90 and 75 per cent oxygen, respectively, a necessary adjunct because gas anesthetics are absorbed so fast from the lungs that there would be no room in the red blood corpuscles to carry oxygen. Cyclopropane with curare is a good combination, permitting relaxation otherwise not obtainable with these agents.

Spinal anesthesia is condemned by many because of its effect on the blood pressure, the capillaries, and the nerve cells. Ephedrine is an excellent drug for the shock that may occur (see Chapter 14). Anoxemia may occur from shock or paralysis of the intercostal muscles if the anesthetic gets up to the fourth, fifth, or sixth cervical segment.

3. *Postoperative.* Anoxemia following operations is usually due to combinations of causes. In general surgery it may be anoxic due to obstruction of air passages, tight binders, anemic due to internal hemorrhage, stagnant due to loss of plasma or dehydration, or combinations. Following chest surgery, it is usually anoxic due to tension pneumothorax, exudate, or transudates but also to obstructions in the tracheobronchial tree.

Effects of Anoxemia.—Man cannot exist without oxygen. In Chapter 13 we define the loss of blood and deprivations of oxygen as the two real emergencies. Not all tissues in the body are equally vulnerable to

pressure begins to fall and the pulse rate increases with variations in the volume of individual beats (Brace syndrome), due to failure of the heart as a result of anoxemia.

The failing heart cannot force blood through the inactive lungs, and there results venous stasis, with prominence of the veins in the neck and nosebleed. There is usually deep cyanosis. Cyanosis is a bluish discoloration of the skin due to the presence of excessive amounts of reduced hemoglobin in the blood of the superficial capillaries (the subpapillary venous plexus). Since oxygen is constantly lost as the blood passes through the capillaries, the oxygen level of the blood will be lowest in the veins. The normal 15 Gm. of hemoglobin per 100 c.c. of blood can take up 20 volumes per cent of oxygen. When hemoglobin gives off oxygen it becomes *reduced hemoglobin* (blue pigment), and since 5 Gm. of hemoglobin absorbs 6.7 c.c. of oxygen, we may say that 5 Gm. of reduced hemoglobin are formed when 100 c.c. of blood give up 6.7 c.c. of oxygen. After 5 Gm. of reduced hemoglobin are formed, cyanosis appears. Therefore, cyanosis is evident when the blood in the capillaries has lost 6.7 volumes per cent of oxygen, that is, when the hemoglobin is 6.7 per cent unsaturated.

Abnormal toxic compounds of hemoglobin may produce cyanosis (methemoglobin and sulfhemoglobin, also the sulfonamides).

Cyanosis may result from anoxia (of the anoxic or stagnant type). It cannot occur in severe anemia with an extremely low hemoglobin concentration (5 Gm. or less).

Blood pressure fails due to cardiac inadequacy and pooling of the blood in the great capillaries and veins, causing shock. In milder types of anoxia there may be great muscular weakness and various mental symptoms, also headache, nausea and lassitude. Later there are vomiting, diarrhea, and mental confusion resembling alcoholic intoxication. If the anoxia is long continued, there will be convulsions and death.

Treatment of Anoxia.—*First of all, the cause of the anoxia must be relieved; then the patient must be forced to breathe by artificial respiration with an ample supply of oxygen.*

Anoxic Anoxia.—Foreign bodies must be removed from the air passages. Sometimes this can be done with the fingers. In a child, one can often dislodge a foreign body by turning the patient upside down. Artificial respiration is useless unless the foreign body is first removed, and if simple measures fail, special apparatus (such as the laryngoscope or bronchoscope) should be employed. However, these may not be available. In this case, tracheotomy should be done. An opening is made in the trachea below the site of obstruction. Artificial respiration may then be instituted. It must be started at once; four to five minutes' delay may be too late. This course of treatment will undoubtedly save lives. If the patient is in an airtight or gas-filled room, he must be moved to the open air. If in water, his lungs must be emptied. Drowning is a common cause of asphyxia. Artificial respiration should be continued for at least an hour. Failure to detect the pulse does not mean that the heart has

emia. The hypoglycemia after some anesthetic agents is said to be due to a cessation of liver function due to anoxemia. Restoration is brought about by inhibition of adrenal cortical secretion and increased production of adrenaline.

Other effects are reduced renal function, acidosis due to lack of bicarbonate shift, which in turn is due to permeability of red cell walls to anions as well as cations; and decreased function of adrenal cortex with disturbances in potassium sodium ratio and which in turn affects water balance, interstitial fluid, and blood sugar level.

Bone marrow effects vary with the degree of anoxemia which is a stimulant to erythrocytosis when mild. Severe degrees of anoxia, however, produce atrophic changes in the marrow resulting in anemia.

Compensatory changes take place in anoxemia as in other bodily injuries, and as in other general traumas (dehydration, acidosis, hemorrhage, shock) the compensatory mechanisms are manifested in a greater or lesser degree, depending upon the time limit. In high altitudes, for example, there is a compensatory polycythemia and erythremia which is first due to a contraction of the spleen, later to anoxic stimulation of the bone marrow. At first there is also a decrease in blood volume and an increased blood flow through the heart. Thus, more red cells pass through the lungs for oxygenation per minute. Yet there has been no actual great increase in the number of cells except those thrown out by the spleen. By the fifth day in high altitude there is an actual increase in red cells and the cardiac output decreases concomitantly with the actual increase in hemoglobin and erythrocytes. Other compensatory mechanisms are: hyperpnea with increased elimination of carbon dioxide, increased amount of glucose in the blood, increase in blood supply to those organs most sensitive to oxygen want.

Symptoms and Signs of Anoxia.—The symptoms and signs of anoxia depend on the type but, in general, are much the same. Symptoms of anoxemia usually begin when the alveolar partial pressure falls to 60 mm. of mercury—the normal being about 100 to 110 mm. of mercury. However, in pathological states where there is a great demand for oxygen, such as hyperthyroidism, infections with high fever, etc., or where it cannot be quickly transported, requirements may be higher and alveolar pressure and oxygen concentration must be kept to high levels in the blood to avoid symptoms and signs of anoxia. In the obstructive type the patient makes futile attempts to breathe, using all accessory muscles of respiration. He becomes alarmed quickly and very early manifests mental disturbances such as extreme restlessness, irritability, exhilaration, delirium, delusions, or he may become maniacal. In other types, breathing is at first stimulated and there is an increase in rate and amplitude and then becomes slower, gasping, and finally ceases. In most types there is at first a slight decrease in pulse rate, with a rise in systolic pressure (stimulation of the cardioinhibitory and vasomotor centers). Soon the

7. Direct mouth-to-mouth breathing, using a handkerchief or piece of gauze, will deliver about 16 per cent oxygen—a method quoted in the Bible and useful in dire emergencies, especially in the newborn.

8. The Sylvester supine position.

Anemic Anoxia.—Anemic anoxia requires blood transfusion. A sufficient amount of blood must be given to transport the oxygen. A common observation is to see a postoperative patient in an oxygen tent, dying of anoxia. There is no cyanosis, but all other symptoms are present. Obviously, hemoglobin, not oxygen is needed.

Stagnant anoxemia means a "standstill" of the blood. Here attention to the heart and plasma to relieve hemoconcentration is the treatment of choice.

Histotoxic varieties of anoxemia may be helped by chemical antidotes, plus oxygen and artificial respiration.

The Use of Oxygen Therapy.—The supply of oxygen controls the sensitivity of the respiratory center. Slight deficiency increases its sensitivity, extreme deficiency diminishes it. However, oxygen deficiency is not the respiratory *stimulus*—this is carbon dioxide, acting through the pH of the blood. The use of carbon dioxide by inhalation in asphyxia is logical because it restores the normal amount of blood bicarbonate and increases breathing. Severe anoxemias will require more carbon dioxide; those less severe require less, because the center is more sensitive. Oxygen therapy in all types of anoxia is an adjunct after the primary cause has been eliminated. It is also indicated in many other states not associated with anoxia, such as coronary occlusion, fevers, migraine, polycythemia, hyperthyroidism; also to eliminate nitrogen from the body, to prevent decompression, sickness or to combat intestinal obstruction.

Oxygen may be administered by the *oxygen tent* or *chamber.* We have a chamber in the Riley hospital with two rooms. It is very efficient but is expensive and requires careful supervision. The tent is equally effective and will deliver up to 60 per cent oxygen. In both types air must be circulated by a fan or the patient will be uncomfortable; also the atmosphere must be cooled. It is difficult to regulate the temperature accurately. The *oronasal* catheter will deliver anywhere from 40 to 70 per cent oxygen, with a flow of 5 to 8 liters per minute. It has the disadvantage of being unreliable and of causing extreme dryness of the upper respiratory passage as well as irritation. The Boothby-Lovelace-Bulbulian (B.L.B.) mask is very efficient and will deliver up to 100 per cent oxygen.

The use of 100 per cent oxygen by inhalation is useful in intestinal obstruction along with decompression; also, at the time of operation, it may quickly restore the normal color of the bowel. Following surgery, oxygen inhalation should not be used as a last resort and for serious complications only. It is useful to minimize postoperative distention

stopped beating, for sometimes its beat is so feeble that it can scarcely be heard with the stethoscope; therefore, the necessity for perseverance.

Where temporary paralysis of the respiratory or cardiac centers occurs, as in electrocution, artificial respiration is urgently needed. If the muscles of respiration are crippled, as in higher anterior poliomyelitis, prolonged artificial respiration is necessary. Here the "iron lung" (the Drinker respirator) must be used. In laryngeal diphtheria an intubation tube, such as the O'Dwyer tube, may be used until such a time as the patient can breathe or tracheotomy should be performed.

The most commonly employed method of artificial respiration is Schafer's method. The patient lies in a prone position, with face to one side. A blanket or coat is placed underneath the abdomen. The tongue is pulled out and, if the patient is unconscious, the jaw will collapse and the tongue will stay out. The operator straddles the patient, with his knees on either side of the patient's knees, and presses with both hands firmly upon the back, over the lower ribs, forcing air and water out of the lungs; then he raises his body slowly and at the same time relaxes the pressure with his hands, allowing the chest wall to relax, thereby creating a negative pressure and causing air to be inspired. This forward and backward movement should be done about every four seconds, or fifteen to sixteen times a minute. Experiments with radioactive sodium show that artificial respiration moves the blood through the vascular system. It has been suggested the heparin be used so that blood will not clot in asphyxia, because as long as blood is moved and artificial respiration is continued, oxygenation may occur.

Other types of artificial respiration are:

1. Manual pressure on a 5-liter rubber bag may be used postoperatively or during surgery with an endotracheal tube. In this way the patient is made to breathe regularly with an adequate supply of oxygen. Too much pressure should not be used because of the danger of atelectasis, congestion, hemorrhagic infiltration, and bronchial spasm—the pressure exerted should not exceed 35 to 40 mm. of mercury, which gives about 29 to 36 mm. of mercury in the bronchiolar system. This may also be accomplished by the automatic machine devised by Craaford and also by Mautz.

2. A two-phase (positive-negative pressure) resuscitator.

3. The Kreeselman bellows.

4. The Neff-Ling apparatus.

5. Drinker respirator.

6. The Eve rocker method—particularly useful in drowning—where Eve believes the helpless diaphragm may be raised and lowered by tilting—10 rocks per minute with a tilt of 50 degrees to ventilate 600 c.c. per rock (normal is 500 c.c.). In favor of this idea is the fact that the lungs of drowned persons often float in autopsy. Much of the water is in the stomach.

significance, although the latter may interfere with function. Rarely the sternum is absent, sometimes it is bifid. *Funnel chest* is the opposite of pigeon breast and instead of a protruding deformity there is a funnel-shaped depression of the anterior chest wall. Other names for this condition are *pectus excavatum, trichterbrust,* and chonechondrosternon. The effect of the deformity on the thoracic viscera is that of compression. The cause of the condition is unknown but is thought in part to be due to obstruction to breathing necessitating an increased amount of pull by the diaphragm, thereby increasing negative pressure and it may also be caused by actual shortening of the diaphragm. Treatment is indicated when symptoms are present. However, if the deformity is pronounced and progressive, surgery is indicated. Early, this consists of resection of the lowest costal cartilages (fused sixth and seventh), division of the xyphoid from the gladiolus, severance of the substernal ligament, and severance of the diaphragmatic attachments from the resected portion of the costal cartilages. This allows the sternum to spring up to its normal position. Late, after the deformity has been present to adult age, the costal cartilages are resected and a wedged transverse osteotomy of the sternum at the level of the second costal cartilage is then performed. The sternum is elevated and then the costal cartilages resutured.

Hernia of the lung (a protrusion of the lung through the endo thoracic fascia together with the pleura) may be congenital or acquired as a result of trauma. The protrusion may not be covered by pleura (evisceration or false hernia). Congenital types may occur in the apices due to funnel chest or anywhere from thoracic defect. One lung may herniate into the other chest due to absence of part of the mediastinum (internal hernia). Rarely, in twins the two chests are connected (thoracopagus) with or without lung hernia.

Treatment consists of correcting the primary deformity as in funnel breast. In congenital absence of part of the chest wall, subperiosteal resection of the ribs may be done and these set at angles in criss-cross fashion to correct the defect.

Injuries of the Chest Wall (Nonpenetrating)

Injuries to the chest wall are common. The danger, as in head injuries, is that of injury to the vital organs within. Contusions and lacerations are dealt with by the same methods as are used for other parts of the body. However, should a laceration penetrate the pleura or lung, the wound should be cautiously cleaned and closed tightly at once in order to preserve the intrathoracic pressure and prevent mediastinal shifting. *Fractures* of the ribs are extremely common; they are sometimes produced by blunt force and often by muscular action, as by sneezing or coughing. If the lung is punctured, it will collapse and give definite symptoms and signs (q.v.). The x-ray will demonstrate fractures but

and postoperative headache. In shock it helps overcome the stagnant anoxia. Pulmonary complications, such as postoperative pneumonia, atelectasis, pulmonary edema, and pulmonary embolism, are greatly helped by the administration of oxygen. Lastly, the inhalation of oxygen is useful in anaerobic infections such as tetanus and gas gangrene.

Oxygen therapy may be dangerous if improperly used. One hundred per cent oxygen given to normal persons at 1 atmosphere for five to six hours may cause pulmonary congestion and edema, a reduction of vital capacity, substernal pain, nose and throat irritations, impaired vision, and rise in blood pressure. If continued for twenty-four hours, it may even cause collapse, and in experimental animals death occurred after thirty-nine hours with pleural effusions and severe injury of the lungs, liver, spleen, and kidneys. Therefore, 100 per cent oxygen should be used for only two to three hours at a time, if at all.

Although it is stated that 100 per cent oxygen may be given for twenty-four hours at a time in severe anoxia, it is perhaps unwise to use it because in such states lungs are already damaged and will react unfavorably. It is also stated that 40 to 50 per cent oxygen is of no value. I am sure that if there is need for it and the primary cause has been eliminated that 40 to 60 per cent oxygen will be very helpful. In severe cases it should be given at 85 per cent concentration under slight (35 mm. of mercury) pressure.

Drugs and Other Agents in Anoxia.—Glucose prolongs consciousness in anoxia due to high altitude flying. Carbon dioxide, 5 to 7 per cent, with 93 to 95 per cent oxygen may be helpful in severe anoxia due to carbon monoxide and for brief periods. Carbon dioxide is useful in anoxia for the following reasons: (1) it is a respiratory stimulant; (2) it increases the depth of respiration and therefore tends to prevent atlectasis; (3) because of the depth of respiration, venous return is augmented; (4) it increases dissociation of carbon monoxide from the hemoglobin.

Drugs such as Adrenaline may be useful in certain kinds of shock (spinal anesthesia, anaphylaxis). Drugs are not readily absorbed as a rule due to the accompanying shock, and respiratory stimulants should be given intravenously if at all (caffeine, sodium benzoate).

In asphyxia neonatorum, the airway must be cleared, spontaneous respiration initiated, and oxygen given. If oxygen is given by endotracheal tube and the blood does not become red, an arteriovenous shunt or massive pneumonia is probably present. If spontaneous respiration does not start, cerebral injury or deep anesthesia of the respiratory center is present.

DISEASES AND INJURIES OF THE CHEST WALL

Congenital anomalies of the chest wall are rare. The more common conditions such as fused or forked ribs, *pigeon breast*, have little clinical

organ within the thorax or the abdomen. In addition, important abnormalities in physiology of respiration may ensue.

Effects of Thoracic Injuries.—The pathological and abnormal physiological effects of the chest wounds may be divided into the following categories: (1) Pathological effects due to the increase in air pressure within the pleural cavity or elsewhere. This air may be merely present or may be present under tension and is known as (a) traumatic pneumothorax, (b) mediastinal emphysema, (c) pneumopericardium, (d) subcutaneous emphysema. If the air in the pleural cavity is under pressure, it is known as a tension pneumothorax. (2) Abnormal mobilities giving rise to (a) mediastinal flutter, (b) paradoxical respiration, (c) mediastinal shift. (3) Abnormal collections of fluid. This may be serum, blood, or pus. If serous, it is hydrothorax; if bloody, it is a hemothorax; and if pus, it is a pyothorax or empyema. The serous fluid is either transudate or exudate. The bloody fluid is due to hemorrhage from intercostal vessels, internal mammary arteries or veins, blood vessels of the lung, or, rarely, major vessels within the thorax. (4) Combinations of the foregoing may produce hydropneumothorax or hemopneumothorax or pyopneumothorax. (5) Injury to thoracic viscera. Lacerations of the lung are not infrequent following nonpenetrating wounds and have been recently well described during World War II as blast injuries to the lung. Syncope and heart damage may occur from nonpenetrating wounds but are more apt to result from those which penetrate. These have been described under the subject of heart injury. Any organ or organs may be injured by penetrating or perforating wounds. (6) Injury to the diaphragm, although far more common with penetrating wounds, rarely may occur in a nonpenetrating injury. (7) Thoracico-abdominal injuries due to gunshot wounds of the chest or stab wounds may injure blood vessels and viscera above and below the diaphragm.

Effects of Abnormal Pressure or Increase in Pressure Within the Thorax.—Air may be present, as has been noted, within the pleurae, the mediastinum, the pericardium, or under the skin. It is also sometimes encountered free in the abdominal cavity from the perforated viscera or from a thoracico-abdominal injury, rarely by finding its way from the thorax into the abdomen along the great vessels. The mere presence of air in an abnormal position is not serious and is only important because of its diagnostic value. However, when air accumulates under pressure in any of the situations mentioned, serious symptoms may result. In the chest such accumulations of air are known as a tension pneumothorax (pressure pneumothorax) or a tension mediastinal emphysema. If the air is in the pleural cavity, it may get there by: (1) An open wound which sucks air; that is, the wound is small or at least smaller than the diameter of the trachea and permits air to be drawn in with each inspiration and to be forced out only partially with each expiration. It is, therefore, a building up of pressure. The same effect could be produced by a flap of

will not show cartilaginous tears at the chondrosternal articulations. These may result in dislocations or slipping ribs. These may be very painful. If anteroposterior pressure is made on the ribs, pain will be referred to the site of injury. The *treatment* consists of blocking the intercostal nerves with 1 per cent Novocain and the use of an elastic binder about the chest. This forces the patient to breathe with the diaphragm, putting the ribs at rest. In complete or multiple fractures with displacement, the fragments should be wired. The sternum is rarely fractured but may embarrass respiration or cause internal injury if much deformity exists. The treatment consists of rest with a sandbag between the shoulders.

If the sternum is so deeply depressed that vital functions are hampered, operative reduction is necessary. The sternum may be held in place by wiring the fragments. Extensive fractures of the ribs and sternum may produce great deformity (stove-in chest) and may be accompanied by severe complications such as mediastinal emphysema, tension pneumothorax, hemorrhage, mediastinal flutter, paradoxical respiration due to flapping chest wall, laceration of lungs, mediastinal hematoma, acute gastric dilatation, an embolism, and, if the trachea or bronchi become obstructed with blood or mucus, massive atelectasis. In all such injuries it is better to wire the fragments together by open operation.

INJURIES TO THE CHEST

The results obtained in thoracic centers during World War II were splendid. In civilian practice the same results have been obtained. At the outset we must take cognizance of the fact that most injuries are combined ones, including head, thorax, abdomen, and lacerations and fractures of the extremities. Therefore, the composite picture produced by the effects of an automobile accident upon a patient may be extremely difficult to interpret. We have touched upon the matter previously in the discussison on shock, head injuries, hemorrhage, and injuries to the blood vessels and the heart. Chest injuries may be divided into three types: (1) nonpenetrating. Such injuries have no external wound and are due to contusions, birth injuries, severe straining, or violent coughing. Although there is no penetration of the chest cavity, serious and dire effects may ensue. (2) Penetrating wounds of the chest which do not have an external opening. Such wounds are usually the result of a fractured rib being driven inward with resultant injury to the pleura, lung, large vessels, thoracic duct, heart, or diaphragm. (3) Penetrating and perforating wounds which are open. Such injuries are produced by bullets, shrapnel, knives, or other implements; also by compound fractures of ribs due to severe contusions with lacerations of the chest wall. The effect of penetrating open wounds depends upon the position of the wound or trajectory of the bullet or foreign body and may involve any

sucking wound must be closed, but, in addition, the tension must be relieved immediately. In civilian practice this is accomplished by the use of a large bore needle to which is attached a long tube which goes beneath a water level at the side of the bed. It is our custom to introduce two such needles, one posteriorly so that fluid as well as air may emerge, the other anteriorly so that air which rises to the top in a patient lying on his back may easily find egress through the large bore needle. The water seal arrangement of course prevents air from being sucked in but permits air to get out. During World War II this same treatment was used but a mobile piece of equipment, namely, a small (No. 16 French) catheter, was introduced into the chest and sealed with adhesive and collodion. Over the end of this tube was the thumb of a rubber glove with its end cut out. This was tied to the tube so that it acted like a flutter valve, permitting air to get out but collapsing during inspiration, thus preventing air from getting in. In this way soldiers with chest injuries could be safely transported to the large hospitals for definitive treatment. Of course, air may be sucked out by actual suction or by other devices, by negative pressure such as Wangensteen suction, water valve suction, etc.

Effects of Abnormal Mobility of the Mediastinum, Shifts of the Mediastinum, and Paradoxical Respiration.—The mediastinum is normally a movable structure which stays in the midline because air pressures within the two pleural cavities are equal even though they may vary during inspiration and expiration. However, should pressure within one side of the thorax vary from that of the other, shifts in the mediastinum may ensue. This is seen clinically in such conditions as massive atelectasis, in which the mediastinum is pulled toward the affected side, and in collections of fluid, blood, pus, or air on one side, pushing the mediastinum toward the normal side. In chest injuries the chief cause for changes in the mediastinum are collections of air or fluid or extensive injuries to the chest wall. With pneumothorax, the mediastinum is pushed over to the normal side and is pulled somewhat by the negative pressure on that side. As we have seen, when air enters the pleural cavity, the lung collapses not only because of the air pressure, but also because of the elastic recoil of the lung. The mediastinum will be pushed to the opposite side and remain more or less in this position. This is known as mediastinal shift. The results of this shift may produce anoxemia for two reasons: (1) It may interfere with respiration on the normal side and (2) it may prevent blood from reaching the right heart due to a twist on the large veins. The latter is probably due to the fact that the mediastinum, in shifting, rotates slightly. With mediastinal shift, during inspiration air rushes into the good lung but cannot enter the affected one. During expiration, air leaves the normal lung and the mediastinum may be pushed to the affected side slightly by an increase in intrapleural pressure in the uninjured half of the chest. In tension

skin or muscle which points inward, permitting air to come in but not to get out. (2) An opening anywhere in the bronchial tree or lung which may permit air to enter the pleural cavity and to build up pressure. The effects of tension pneumothorax are as follows: As a result of the increase in intrapleural pressure and due to the elasticity of the lungs, there is a complete collapse of the lung on the affected side. In addition, the mobile mediastinum is pushed over to the opposite side due to the fact that pressure is much greater in the injured pleura and also because a negative pressure is present on the unaffected side. This is known as *mediastinal shift.* Sometimes there is enough air pushed out with every expiration and enough sucked in with inspirations that tension pneumothorax does not occur. In this case the opening is larger than the trachea and air gets in and out with respiration. However, the air pressure within the pleural cavity is equal to atmospheric pressure, whereas the pressure in the unopened pleura is below atmospheric pressure. The effects of this situation are a collapse of the lung on the open side and a shift of the mediastinum which moves back and forth, moving toward the intact half during inspiration and toward the open pleura during expiration. This is known as *mediastinal flutter.* The effects of mediastinal shift and flutter will be discussed in some of the following paragraphs.

The physiology of respiration with changes in air pressure in the pleural cavity is altered as follows: With pneumothorax, air goes into the good lung with inspiration but does not get into the collapsed lung because the intrapleural pressure is increased and the lung is collapsed even more, so that any air which may be present in this lung is shifted over to the other side. With expiration, air leaves the good lung and some air leaves the pleural cavity of the affected side, therefore lessening the intrapleural pressure; thus some air from the unaffected lung finds its way into the opposite lung. This is paradoxical respiration and will be discussed further in subsequent paragraphs. It should be said here, however, that the little air which is exchanged under the conditions described in the lung on the affected side is impure and therefore does not contribute to the oxygenation of the blood. In tension pneumothorax, with every inspiration, air pressure within the pleural cavity becomes greater, collapsing the lung completely and pushing the lung far toward the unaffected side. In this case no air gets into the collapsed lung, and due to the great shift of the mediastinum, there is a diminished amount of air entering the normal side. If the mediastinum or lung is fixed by adhesions, the effects would be minimized. Mediastinal emphysema is important because it prevents the blood from returning to the right heart. In this way stagnant anoxemia is produced and shock develops very rapidly due to diminished return of blood to the heart, with resultant cardiac inadequacy. Pneumopericardium behaves very much as cardiac tamponade. This has been discussed previously under heart injuries. The treatment of pneumothorax depends upon its cause. Obviously a

anoxemia. The treatment for abnormal mobilities is to correct the cause. Open wounds should be closed and flail chests supported by padding and elastic straps. In addition, the patient should be on the affected side to delimit movement. Should symptoms persist, open operation with wiring of rib fragments should be done.

Abnormal Collections of Fluid.—Following injuries to the chest, transudates and exudates may appear within the lung or the pleural cavity or both. In addition, hemorrhage may occur.

Fluid Within the Lung.—Fluid within the lung or pulmonary edema is so common following chest injuries that it has been termed traumatic wet lung. Many theories have been advanced to account for this phenomenon. No doubt many different factors are at work, depending upon the type of injury. It is easy to understand how blast injuries, contusions, and penetrating and perforating wounds of the lung may cause transudation and exudation of the fluid and blood. The uninjured lung is wet also; this has been thought to be due to immobility and stasis with passive congestion; also bronchial and tracheal occlusions with mucus and blood, causing partial atelectasis with dyspnea. To prevent these factors from operating, the intercostal nerves are injected with Novocain along the injured area to stop reflex respiratory inhibition, and frequent tracheal aspirations and bronchoscopy are used to remove mucous plugs. Anoxemia, whether anoxic or stagnant, may invite transudation in the lung. Unconscious patients who lie in one position invite hypostatic congestion which may be conducive to wet lungs. Furthermore, they develop tracheobronchial obstruction due to mucous plugs. For this reason tracheotomy is frequently done in head injuries. One more factor is that of a very tight thoracic bandage which prevents expansion.

Fluid in the Pleural Cavity.—In the pleural cavity very much the same factors are at work. In addition, most chest wounds are accompanied by some form of intrathoracic injury which gives rise to hemothorax. The presence of blood in the pleural cavity or of fluid interferes with respiration on the affected side and causes a collapse of that lung. If large enough, the mediastinum may be pushed over to the opposite side, and since usually fluid is associated with air as a hemopneumothorax or hydropneumothorax, the combined effect is one of great pressure.

It was formerly thought that blood in the chest did not clot. This is still true, but it is supposed that the reason blood does not clot in the chest is due to the fact that it is defibrinated and that the fibrin is whipped out by respiration and deposited on the visceral and parietal pleurae. Thus the defibrinated blood does not clot. Bleeding in the chest may occur from various sources; namely, intercostal vessels, the lung, internal mammary vessels, and large thoracic vessels. Physical signs and symptoms and x-ray examination reveal the presence of fluid. Thoracentesis tells us whether the fluid is primarily serum or blood.

pneumothorax the mediastinum may be pushed over so far to the opposite side that aeration cannot take place in the good lung due to compression by this structure and, moreover, blood cannot enter due to air pressure or to a shift in the position of the large veins. It is apparent that in the latter condition, if the tension pneumothorax is on the right side, pressure of the air alone may occlude the vena cavae which may also be compressed by the shift. If the pneumothorax is on the left side, the shift and the twist mechanically occlude the large veins. In either event, there results anoxemia which is both anoxic and stagnant, and early shock and death will ensue unless the condition is promptly corrected.

If the mediastinum shifts from side to side with respiration, a condition known as *mediastinal flutter* results. This is seen chiefly in two conditions: (1) open chest wounds in which the diameter of the wound is as large or larger than that of the trachea and (2) stove-in or flail chest. In the previous discussion we described the effects of these conditions. Here we are interested chiefly in the effects on the mediastinum. With an open wound in the chest, with inspiration the good lung will expand. The injured pleural cavity, filled with air at atmospheric pressure, will draw in more air. The effect of this is to collapse the lung on the injured side and to shift the mediastinum to the opposite chest. During expiration the uninjured lung contracts as air leaves the lung. Air also leaves the injured pleural cavity, and the mediastinum is thereby permitted to swing back toward the injured side of the chest; air leaves the injured lung during inspiration and crosses to the good side, whereas air leaves the good lung to enter the injured lung during expiration, slightly inflating the latter. The to-and-fro shift in the mediastinum is known as mediastinal flutter. This may be very serious because of interference with circulation or the return of blood to the heart and interference with respiration. The second cause of flutter is due to paradoxical respiration, the result of a crushed chest, in which with every inspiration the chest wall is sucked in and with every expiration it is expanded. On the uninjured side normal movements prevail. The chest wall expands during inspiration and contracts during expiration. The effect of the paradoxical movement on the injured lung and mediastinum is as follows: During inspiration there is a contraction of the injured side, compressing the lung and pushing the mediastinum over toward the normal half of the chest which expands normally. Very little air enters the collapsed lung; in fact, air leaves it and crosses over to the normal lung. During expiration the injured chest expands due to increased intrapleural pressure, but the lung is inflated very little and this is due to air passing over from the good lung, which has just contracted, pushing the mediastinum over toward the injured side. Mediastinal flutter is not as pronounced as in open wounds of the chest, but the combined effects of the flutter and lack of air on the injured side with a decrease in respiration of the normal side (due to the abnormal mediastinal movements and the to-and-fro movement of air which is not oxygenated) will produce

anoxemia. The treatment for abnormal mobilities is to correct the cause. Open wounds should be closed and flail chests supported by padding and elastic straps. In addition, the patient should be on the affected side to delimit movement. Should symptoms persist, open operation with wiring of rib fragments should be done.

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The treatment of hemothorax and of serous collections is that of aspiration which may be repeated. Fresh hemorrhage is not caused unless strong negative pressure is produced. This should be done early and not replaced with air. If blood is present, it may be aspirated and retransfused into the patient after mixing it with citrate solution. Following aspiration the patient is watched carefully. If blood accumulated quickly and if there is a fall in the hematocrit, it may be assumed that a large vessel has been torn. This would demand *thoracotomy*. If, however, the lung expands after aspiration and no signs or symptoms of shock appear, the bleeding has stopped and further interference will not be necessary. In those cases of hemothorax with a persistent shadow on the x-ray film, fever, and negative results from aspiration, it may be assumed that a thick fibrinous exudate is present over the lung, preventing its expansion. This would require visceral *decortication* which permits re-expansion of the lung and prevents chronic empyema.

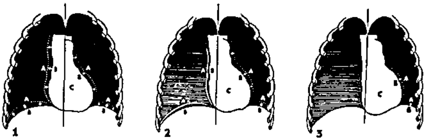


Fig. 213.—Diagrams illustrating fluoroscopic movements in the thorax.

1. Normal movements of the diaphragm and mediastinal border during (a) expiration diaphragm elevated and mediastinal shadow widened) and (b) inspiration (diaphragm lowered and mediastinal shadow narrowed).

2. *Empyema before localization has occurred. Movements normal on the* unaffected side. Movements exaggerated on the affected side, with movement of the lower lung margin if the empyema is not massive. If part of the fluid is aspirated, these movements are more easily observed.

3. After localization the diaphragm, mediastinum, and lower lung margin do not move, whereas movement on the unaffected side is exaggerated. In massive empyema some of the pus is aspirated, so that fixation by pressure may not be mistaken for localization by a pyogenic membrane. (From Berman, J. K.: J. Indiana M. A. 29: 419, 1936.)

The operation of visceral decortication was popularized during World War II. Extensive studies on patients with *fibrinous hemothorax* have shown that this deposit of fibrin, infected or uninfected, should be removed. The operation is done through the sixth interspace. After the chest has been opened, the pleural cavity will be found to contain blood clot, pus, and shaggy purulent fringes hanging from the pleura. A line of cleavage is easily established and the deposit on the visceral pleura is removed. The parietal pleura deposit is also removed so that two pleural surfaces may adhere. The lung can be easily expanded by the anesthetist through the endotracheal tube. Any lacerations which are encountered in the lung are sutured. The optimum time for this procedure is between ten and twenty-five days. Earlier than this the decortication may start bleeding again. Later than this the fibrinous coat becomes organized with a layer of granulation tissue beneath it so that stripping leaves a raw bleeding surface which may be conducive to a recurrence of the hemothorax. *After the chest*

is closed, two small tubes are inserted, one in the third interspace anteriorly, the other in the seventh interspace in the posterior axillary line for underwater seal drainage. These are removed after about forty-eight hours.

Injury to the Viscera.—In Chapter 18 we discussed injuries to the heart. In this discussion we spoke of syncope and heart damage from contusions; also perforating wounds of the heart were discussed; therefore, heart injuries will not be included in this résumé. The lung is frequently injured and usually does not require suture. However, large lacerations would require open thoracotomy with suture. Infrequently, large vessels are torn which may require suture or even ligation. Smaller vessels are tied. The thoracic duct may be injured and this may result in chylothorax. This has been discussed in Chapter 18. Last, abdominal injuries frequently occur in connection with thoracic wounds. In civilian practice we have encountered perforations or lacerations to the following abdominal organs in connection with thoracic injuries: stomach, pancreas, liver, kidney, spleen, hepatic flexure of the colon, and inferior vena cava. In most of these injuries transthoracic approach was used. The diaphragm was opened widely and the injured organ sutured or removed. The diaphragm itself is frequently torn. This occurs sometimes in nonpenetrating injuries and is probably due to strong abdominal force together with a compression of the lower chest. Usually, however, the injury is produced by projecting ribs or by a knife wound, resulting in a large opening in the diaphragm with protrusion of abdominal viscera into the thoracic cavity. Such injuries require thoracotomy and repair of the diaphragm. Sometimes it is advantageous temporarily to interrupt the phrenic nerve by the injection of Novocain or by crushing so that the diaphragm may be immobilized to facilitate repair and healing.

Anesthesia.—One of the most important persons of the team doing thoracic surgery is the anesthetist. Endotracheal anesthesia is employed in all thoracic or thoracico-abdominal injuries. The anesthetic agent may be cyclopropane or nitrous oxide and curare or ether. We prefer the latter. In fact, it is the best all around anesthetic agent for injured persons. This, added to the fact that most of these patients have had great loss of blood, producing severe anemia, makes ether the only anesthetic which can give full relaxation. (See Chapter 13.)

Complications and Sequelae of Chest Injuries.—We have already seen that the chest wall may be deformed or destroyed, permitting in the latter case hernia of the lung. This complication can be corrected by using portions of adjacent ribs to bridge the gap and stabilize the chest wall. Inside the chest the pleura may become infected with resultant empyema. When due to hemothorax, decortication should be done. If, however, the empyema is a late development or has been neglected over a long period of time, open drainage may be necessary as described under the subject of empyema. Should this form of treatment

fail to obliterate the cavity, visceral and parietal decortication may be tried to permit reexpansion. If this fails, the parietal pleura is removed and the cavity filled in by skin and muscle flaps obliterating it.

Another complication of chest injuries is lung abscess. This will be discussed later. However, here should be mentioned the possibility of this disease resulting from penetrating wounds, contusions, aspiration of foreign bodies, and atelectasis due to obstructions. Abscess is treated by outside drainage as soon as it is discovered. Should the lung abscess become chronic, lobectomy or segmental resection may be necessary.

In open perforating wounds, bronchopleural fistula may result. These usually close spontaneously. Rarely it is necessary to close them surgically. Another type of fistula occurs very infrequently. This is the

Fig. 214.—Hemothorax with fibrinous empyema treated by visceral and parietal decortication. The patient was a man 45 years of age who received a gunshot wound of the right chest. On admission to the hospital the patient was in a moderate state of shock. Physical examination showed the presence of a large amount of fluid in the right chest. This was confirmed by x-ray studies. The patient was treated by blood replacement for forty-eight hours and then 1,500 c.c. of bloody fluid were aspirated from the right thorax. This was repeated at intervals over a period of four weeks. After this time no fluid could be obtained by thoracentesis; however, the patient had a septic type of fever. X-ray examination at this time showed the presence of a fibrinous type of empyema. *A*, Preoperative x-ray film. *B*, Postoperative x-ray photograph taken after visceral and parietal decortication. The lung has almost completely re-expanded.

It is not necessary to do a parietal decortication in the early cases, that is, the hemothorax cases with secondary fibrinous empyema which are within the six to eight-week period. Here a visceral decortication followed by re-expansion of the lung will give good functional results and the lung will remain out. In older cases and in those due to tuberculosis where the visceral and parietal pleurae are thickened, particularly the latter, it is desirable, although oftentimes it cannot be accomplished, to remove the parietal as well as the visceral pleura. The reasons for this are (1) it is easier to get a line of cleavage and (2), if the visceral pleura is removed and the lung is re-expanded, it may not stick to a hard, sclerotic, thickened pleura which has the consistency of cartilage.

The function of the re-expanded lung in chronic cases, whether tuberculous or nontuberculous, is not as good as might be expected from the x-ray picture. Its respiratory function is greatly decreased although it does have a space-filling function which obliterates dead space and thereby, eliminates chronic infection. Therefore, it is a desirable procedure.

In the tuberculous varieties of empyema the lung will re-expand after decortication although it may not regain its respiratory function. Furthermore, the old lesions may be activated by the expansion of the lung. A combination of decortication and thoracoplasty may be desirable in some of these cases.

tracheoesophageal communication due to a perforating wound. This complication tends to heal spontaneously but is usually accompanied by an empyema. Sometimes surgery is necessary to effect a closure. Obviously, if such an injury is discovered early, it should be closed at once. In all fistulas and in abscesses the presence of a foreign body should be suspected and if present should be removed.

Summary of Chest Injuries.—From the foregoing discussions one may see that the correct diagnosis and treatment of chest injuries is by no means a simple matter. The difficulties arise in part from the fact that the diagnosis may be very complicated. This in turn is due to the fact that chest injuries are rarely the only injuries that have been sustained. In civilian practice the automobile shows no distinction between the head, thorax, abdomen, and extremities. Head injuries, as we have seen, are accompanied during the stage of stimulation from increased intracranial pressure by a slowing pulse and a rising blood pressure. Contrast this with shock, due to loss of blood, interference with circulation, or anoxemia. In all of these conditions there is a rise in pulse rate and a fall in blood pressure. Yet in patients with concomitant head injuries clinical symptoms and signs may be confusing. In thoracic injuries very often there is an ipsilateral spasticity of the rectus muscle. This may lead to the erroneous conclusion that there has been a thoracicoabdominal injury. Therefore, thoracic injuries must be viewed in the light of the patient as a whole. In order to arrive at a correct diagnosis and to give the correct treatment, the following routine should be observed: (1) thorough and complete physical examination; (2) careful watching of the patient for all changes in temperature, pulse, blood pressure, state of consciousness, control of emunctories, and respiration; (3) hematocrit and plasma protein determinations at frequent intervals; (4) x-ray examinations of the chest and abdomen; (5) thoracentesis and, if indicated, paracentesis; (6) explorations if indicated.

A summary of the treatment would be a summary of the injuries. In general, however, there must be the closest observation to determine proper treatment. A general rule to follow is to arrest hemorrhage first and then treat the patient for shock. Since in chest injuries the hemorrhage may be concealed and shock may result not only from hemorrhage but also from interference with respiration and circulation, it becomes necessary to differentiate the type of hemorrhage and the kind of shock; consequently it is our custom to try to stop external bleeding and to replace blood lost in the chest by autotransfusion. Should bleeding persist as shown by repeated aspirations and progressive fall in hematocrit, an open operation to arrest hemorrhage becomes imperative. In addition, since shock may be caused by tension pneumothorax, mediastinal shift and flutter, and large accumulations of serum or blood, these conditions must be corrected as previously indicated.

Our routine is as follows: Sucking wounds are closed. If tension pneumothorax is present, needle aspiration and drainage are instituted and plasma is started. From this point definitive treatment depends upon the type of injuries present. In all cases, multiple transfusions are given and careful attention is given to water balance and oxygen requirements. Thoracotomy is indicated in large lacerations going into the chest, thoracico-abdominal injuries, uncontrolled hemorrhage, large lung lacerations, and removal of foreign bodies. Following operation or primary treatment we attempt to improve tracheobronchial drainage to prevent atelectasis and pneumonitis. This is done by catheter suction, bronchoscopy, and intercostal nerve block with procaine (to permit normal breathing) and by encouraging the normal cough reflex; also by the use of oxygen and antibiotics.

INFECTIONS OF RIBS

Infections of the ribs may occur as complications. Osteomyelitis may be part of a multiple osteomyelitis (see Chapter 21) or an empyema. Tuberculosis of the ribs and sternum, involving the cartilage, is usually secondary to the disease elsewhere. Its "cold" and insidious development makes diagnosis difficult until draining sinuses appear. The rare typhoid rib is usually a complication of a milder "walking" type of the disease. The treatment is conservative unless sequestra form, in which case they are removed. X-ray is useful in the treatment of tuberculous ribs.

TUMORS OF RIBS

Tumors are benign, such as chondroma, which may be removed; malignant, such as multiple myeloma, in which many bones are involved; or metastatic carcinoma, especially from the breast. In these, x-ray is the only available treatment.

THE PLEURA

Injuries to the pleura have been discussed previously.

Inflammations of the Pleura

Mesothelial structures have many similar characteristics as well as a common origin. Such structures as the pleura, pericardium, peritoneum, synovial membranes (mesenchymal epithelium), bursae, and tendon sheaths line cavities. This lining is one cell layer thick and rests on a basement membrane around which is a layer of fat which is liberally supplied with blood vessels and especially with lymphatics. Mesothelial membranes secrete a thin protein fluid which varies in density (the density is greater in joints and bursae, less in pleura and peritoneum). The capillaries are more permeable than elsewhere and therefore lose more protein, but the lymphatics are well able to absorb this material normally.

The reaction of mesothelial tissues to trauma and infection is rapid and extensive, accounting for the relatively high immunity which they possess. In fact, the entire pleura on the affected side or the entire peritoneum takes part—not a limited area. Any tissue that is traumatized is stimulated to react, and such stimulation to *these* tissues causes an increased secretion of fluid. *This is a protective mechanism, causing immobilization, separation of raw surfaces, dilution of toxins, and, because, of excessive osmotic index, prevention of absorption.* Should injury continue, there would be decreased stimulation and slow absorption of fluid, and the dry, raw surfaces would ultimately become adherent.

In infections of mesothelial tissue the same defense mechanism present elsewhere asserts itself: plasma is lost, due to increased capillary permeability; the osmotic index of the tissue fluid increases, preventing reabsorption; the blood capillaries and lymphatics become thrombosed; cellular exudates form an extensive pyogenic membrane; and local immunity becomes established. In addition, the volume of exudates is prodigious, diluting toxins; floating cells give rise to macrophages, also small lymphocytes, which in turn may give rise to fibroblasts.

Therefore, the treatment is the same as elsewhere in spreading inflammations: rest, waiting for localization, incision, and drainage. In the case of these cavities, the excessive pus and exudates make an excellent irrigating fluid. If untreated, absorption begins after clot retraction in the lymphatics; however, this occurs after eight to ten days, when the exudate is practically sterile and therefore not as harmful. Mesothelial tissues heal very quickly. In the peritoneum, a protective exudate is present within thirty minutes. This prevents leakage in intestinal surgery, for no sutures would be close enough to be watertight and airtight.

Inflammation of the pleura is known technically as *pleuritis,* or *pleurisy,* and may occur as a distinct entity or in connection with diseases of the lung or injuries to the chest. Not all fluid in the chest is due to an inflammation of the pleura (exudate). Hemothorax and chylothorax, from injuries to the large blood vessels or the thoracic or right lymphatic duct and, in the latter instance, malignancy, may play a role, giving rise to blood and lymph within the thorax. Indeed the esophagus may be injured or eroded, giving rise to saliva or food within the chest. In any case, the pleura soon becomes inflamed too and thus hemothorax may be difficult to distinguish from hemorrhagic pleurisy with effusion, especially when there has been no penetrating wound. Last, transudates constitute another cause for fluid in the chest, as seen in cardiac decompensation or constrictive pericarditis, nephritis with edema, mediastinal tumors—this fluid is known as hydrothorax. It is perhaps safe to say that in pneumonia or pulmonary tuberculosis the pleura is usually inflamed. However, these inflammations are a part of the underlying disease and usually improve with it. *Dry* pleurisy (sicca or fibrinous) produces a friction rub which

is heard through the stethoscope and which causes pain with every inspiration. Here the two layers are covered with a fibrinous exudate which rubs and irritates the sensitive visceral pleura. It is usually associated with or is the forerunner of pneumonia or pneumonitis, often with bronchitis or upper respiratory infections, rarely as a distinct and separate entity. It may be tuberculous in origin as discussed in Chapter 8. The causative organisms are pneumococcus, streptococcus, staphylococcus (rarely), and the tubercle bacillus. *Wet* pleurisy is probably a further development of dry pleurisy and is a conservative act on the part of nature, separating the pleural surfaces and in a measure putting the lung at rest. The causes of wet pleurisy (pleurisy with effusion) are variable and the type of fluid is not always indicative of the etiological agent. We have repeatedly shown that with the advent of penicillin, the sulfonamides, and streptomycin, fluid which might have been purulent remains clear. However, it is convenient to classify effusions according to their characteristics which may be as follows:

1. Serous serosanguineous, serofibrinous. These are exudates with specific gravity above 1.012 and transudates are due to (1) the spread of an inflammatory process in the lung, (2) obstruction of a bronchus, (3) obstruction of an artery supplying a pulmonary segment. The inflammatory lesions causing serosanguineous fluid are usually streptococcal but may be due to mixed infections, virus pneumonia, tuleremia, and pyogenic organisms, although the latter usually give rise to purulent or serofibrinous effusions. Serous effusions may be due to nonspecific organisms which have been inactivated by penicillin but almost always a clear straw-colored effusion is due to *tuberculosis until proved otherwise.*

Obstructions to a bronchus may be due to carcinoma, primary or secondary, lymphoblastoma, bronchial adenoma or other endobronchial neoplasms, inflammatory exudate or stricture (tuberculosis, nonspecific as seen in bronchiectasis), foreign bodies. In other words, occlusion from within the bronchus or disease of its walls or external pressure may cause a pleural effusion.

Carcinoma: The intrathoracic carcinomas are bronchiogenic or mediastinal. Secondary growths are due to carcinoma of the breast, ovary, kidney, stomach, colon, etc.

An artery may be obstructed by embolism or neoplasm, giving rise to serosanguineous effusions. Transudates which are all serous may be due to congestive heart failure, constrictive pericarditis, cirrhosis of the liver, and chronic nephritis with nephrosis.

A final group are due to trauma with or without penetration and perforation and also that which follows artificial pneumothorax in the treatment of tuberculosis.

2. Hemorrhagic fluid may be due to injuries or spontaneous hemopneumothorax (due to tuberculosis) or neoplasm of the pleura. Some-

times it is seen in lymphoblastoma, congestive failure, cirrhosis of the liver, pneumonia, and infarction.

3. Chylous fluid is seen in injuries to the thoracic or right lymphatic duct or carcinoma involving them, rarely to congenital anomalies, filariasis, Hodgkin's disease, tuberculous glands, aortic aneurysm, and thrombosis of the subclavian vein. (See Chapter 18.)

4. Purulent fluid (empyema) is due to nonspecific organisms, rarely to tuberculosis or mixed infections (tuberculous and pyogenic). Breath sounds are diminished, there is dullness on percussion, and vocal fremitus is diminished or absent. As the underlying lung condition improves, the pleurisy usually improves also. Occasionally the fluid accumulates in such quantities that respiration is embarrassed by its presence. In this case, *thoracentesis*, or aspiration of the chest, is done with a syringe and needle. X-ray is of help in diagnosis.

Diagnosis of the cause of the effusion is made by a careful examination of the patient after recording his history and then x-ray examination. After this, thoracentesis is done. The fluid is examined carefully. This includes smears, cultures, centrifuging for cells (button), and guinea pig inoculation. Immediately after thoracentesis, x-ray and fluoroscopic studies are continued to determine whether or not the primary disease is in the lung or mediastinum.

The treatment of pleural effusions will depend upon their cause. Tuberculous effusions are discussed in Chapter 7. Those due to other types of inflammation are treated by aspiration or drainage as described in the following discussion on empyema. Fluid due to bronchial obstructions and carcinomas will persist unless the primary cause is eradicated. However, repeated aspiration relieves the patient greatly, permitting him to breathe and thereby relieving the anoxemia. Transudates from other causes are aspirated to relieve respiratory distress and to prevent empyema. Traumatic effusions have been discussed and chylous effusions are described in Chapter 18. In general, it is unwise to leave fluid within the pleural cavity because it interferes with respiraiton and may become secondarily infected and whether it does or not, fibrinous deposits with thickened pleurae result. In tuberculosis, obliterative pleuritis (adhesion between visceral and parietal pleura) is undesirable, and therefore partial aspiration is done. In addition, removal of fluid permits more accurate diagnosis by (1) x-ray and fluoroscopic examination of the lung and mediastinum and (2) careful analysis of the fluid. Pleural effusions decrease plasma proteins and invite dehydration. Hemothorax means loss of blood. Therefore, it is necessary that careful attention be given to fluid and protein balance as well as to blood volume. Empyema is a special type of pleural effusion and is discussed in the following paragraphs.

Empyema.—Sometimes the pleural disease overshadows in importance the causative lung condition. The pleura becomes inflamed and suppuration occurs. This disease is known as empyema thoracis. It is

usually acute and may occur as a complication of pneumonia (synpneumonic) or as a sequel (metapneumonic or postpneumonic). Since the introduction of penicillin and the sulfonamides, the incidence of the disease seems to be less, and, when it occurs, it is less virulent. It is caused by various organisms. The most virulent is the streptococcus (in the synpneumonic form), which invades connective tissue planes within the lung and continues out into the pleura, causing a spreading cellulitis (see Chapter 5). The pneumococcus usually causes the metapneumonic form and is much less virulent. *The staphylococcic form is fortunately* very rare; when it occurs, it is extremely virulent. In any of these the pleura becomes inflamed and edematous, and soon the entire pleural cavity is filled with thin (streptococcic) or thick (pneumococcic) pus. Should the pus burrow to the outside, or into other organs, it is called *empyema necessitatis*. The diagnosis is not difficult in the metapneumonic types but is in the synpneumonic. In the former the history is clear.

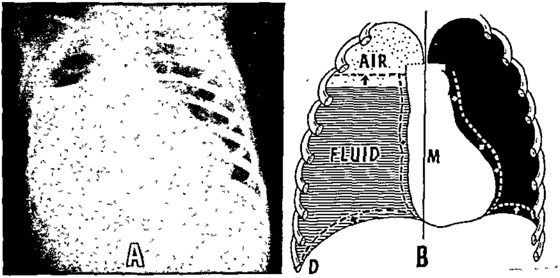


Fig. 215.—The diagnosis of empyema by fluoroscopic examination. Empyema of right pleural cavity. The child is in the upright position. Fixation has not occurred. *A*. X-ray photographs, posteroanterior. *B*. Diagram illustrating fluoroscopic observations. Both leaves of the diaphragm and both sides of the mediastinum move with respiration. As the diaphragm descends on inspiration, the fluid level moves down, and on *expiration* it moves upward. (From Berman, J. K.: Surg., Gynec. & Obst. 76: 183, 1943.)

There has been a pneumonia. The patient's temperature *had returned* to normal but has risen again, assuming a septic character. Percussion reveals dullness, absence of vocal fremitus (which had been increased during the pneumonia, due to consolidation), and absence of breath sounds. The x-ray is indispensable in diagnosis, as is also the aspiration of some pus for smear and culture to determine the type of organism at fault. The prognosis is good in pneumococcic empyema but is more serious in the streptococcic variety and most serious in *the staphylococcic type*.

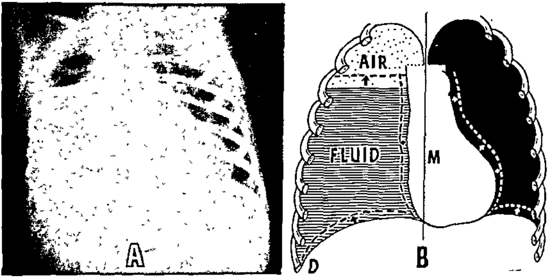
The *treatment of empyema* will vary, depending on (1) its cause (traumatic or *nontraumatic*), (2) the causative organism (nontubercu-

lous, tuberculous, anaerobic), (3) the type of exudate (serous, hemorrhagic, purulent), (4) the extent of involvement (unilateral, diffuse, interlobar, localized, and bilateral).

Before discussing the various types and their treatment, it is well to consider the behavior of fluid in the chest. The systemic effects result from (1) the infection, (2) anoxemia, (3) anemia, (4) hypoproteinemia, (5) dehydration, all of which have been previously discussed in infections in general and also in diseases and injuries of the chest. The local effects are due to: (1) Fibrinous, purulent, or other deposits on the visceral or parietal pleura, more on the latter, but more important, the former, which compresses the lung, making it atelectatic. No matter what type of exudate, the fluid compresses the lung by its quantity. However, very soon a fibrinous deposit on the pleura prevents re-expansion, even if the fluid is withdrawn. (2) The formation of pockets due to the conversion of granulation tissue into fibrous tissue—inflammatory cysts. (3) Adhesive pleurisy, complete or partial.

Medical Treatment.—Medical treatment of empyema includes repeated aspirations, the introduction of penicillin or streptomycin or both into the empyema cavity, relief of atelectasis by bronchoscopic aspiration, systemic penicillin and sulfonamide therapy, attention to water and protein balance, and blood transfusion as indicated. As soon as fluid is discovered in the chest, it is aspirated and studied as outlined in preceding paragraphs. Then x-rays of the chest are made again. Fluoroscopic observation as outlined below is invaluable for diagnosis and for treatment. Daily thoracentesis should be done with the injection of 5 to 10 c.c. penicillin, 1,000 units per cubic centimeter, depending on the size of the cavity. By this method an empyema may be rendered sterile and if done early with persistence, the lung may expand and the cavity thereby obliterated. Thoracentesis without the injection of penicillin has been used for many years with good results in some cases. However, the cavity must be obliterated or it will become reinfected. Thus an inflammatory cyst might remain following what appears to be a complete cure of the inflammatory process. That has been a common observation. Here is what happens. When an empyema exists for just a short time and it is aspirated and penicillin has been used, complete resolution may occur; there are many authentic reports of such cases. However, in such patients it might have occurred without the use of penicillin due to repeated aspiration, or it might have occurred without any surgical treatment if we exclude aspiration as a surgical maneuver. But if any length of time transpires between the onset of the disease and the evacuation of the pus, then a pyogenic membrane or a leucocytic barrier is built up. That is granulation tissue, and the longer the delay in healing, the greater amount of this tissue. Granulation tissue goes through stages and finally becomes fibrotic. It becomes a scar, a very thick scar. That scar contracts; nature will not tolerate dead space so that dead space fills up with some-

usually acute and may occur as a complication of pneumonia (synpneumonic) or as a sequel (metapneumonic or postpneumonic). Since the introduction of penicillin and the sulfonamides, the incidence of the disease seems to be less, and, when it occurs, it is less virulent. It is caused by various organisms. The most virulent is the streptococcus (in the synpneumonic form), which invades connective tissue planes within the lung and continues out into the pleura, causing a spreading cellulitis (see Chapter 5). The pneumococcus usually causes the metapneumonic form and is much less virulent. The staphylococcic form is fortunately very rare; when it occurs, it is extremely virulent. In any of these the pleura becomes inflamed and edematous, and soon the entire pleural cavity is filled with thin (streptococcic) or thick (pneumococcic) pus. Should the pus burrow to the outside, or into other organs, it is called *empyema necessitatis*. The diagnosis is not difficult in the metapneumonic types but is in the synpneumonic. In the former the history is clear.



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The treatment of empyema will vary, depending on (1) its cause (traumatic or nontraumatic), (2) the causative organism (nontubercu-

atelectasis which is due to compression by the fluid as well as bronchial obstruction. If atelectasis persists, a residual cavity may be prevented by a pulling in of the chest wall and pulling over of a labile mediastinum. If the mediastinum is fixed, a space will remain between the atelectatic lung and the chest wall which will result in a chronic empyema if not detected. The treatment for an acute empyema which does not readily respond to medical management as determined by daily fluoroscopic studies is open drainage. The same is true for the persistent cavity.

Surgical Treatment.—A pleural infection behaves very much like pyogenic infections elsewhere, and as we shall see after the peculiarities of thoracic physiology are discussed, is amenable to the same forms of treatment as govern the foregoing. "A study of the pathology teaches one lesson in particular—that if the functional value of the lung is to be retained the septic process must be relieved at as early a stage as possible." (Fraser). Resolution may occur and does so in many instances. More commonly, localization takes place, in which event an abscess cavity is formed. Less often the infection is disseminated, giving rise to general septicemia and death.

During normal inspiration the diaphragm descends and the mediastinum is slightly narrowed. During expiration the reverse is true. In the child the mediastinum is a very movable structure easily affected by changes in intrathoracic pressure. The child also has a lower vital capacity than the adult. The child's lungs almost fill the entire pleural cavity. Normally the thorax grows away from the lung with increase in age, leaving a small pleural space. Consequently, the elastic recoil of the lung will be less in the child than in the adult, and therefore intrapleural tension in the child rises to zero at the end of expiration, whereas in the adult it remains below zero.

Dr. John Fraser, of Edinburgh, has demonstrated intrapleural pressure in a conclusive manner. He introduced a hollow aspirating needle of large bore (15 gauge) into the pleural cavity and attached it by a tube to a manometer. In this way he could accurately record pressures. He found that normally in a child of five years there is a range from minus 2 mm. Hg with expiration to minus 6 mm. with inspiration. In adults it is *more negative. In an empyema without walling in, and therefore without fixation of the mediastinum, the diaphragm, and the lower lung, there is a very wide fluctuation, the pressure varying from minus 5 mm. at inspiration to plus 10 mm. at expiration. However, after localization has occurred, the intrapleural pressure remains positive, with very little fluctuation, the pressure ranging from plus 5 mm. Hg to above plus 8 mm.*

This is a very important observation and clearly explains the surgical pathology of empyema. The intrathoracic space is increased by the displacement of the mediastinum and the descent of the diaphragm. This mediastinal displacement occurs very early in children and is due not only to a pushing over, but also to a "sucking" over by the heavily breathing lung of the other side. But after fixation occurs, there is little or no move-

thing and that "something" in this case is usually serum. It is sterile but it is apt to be infected over and over again and it is a menace. Although we may sterilize the cavity, the cavity does remain and will continue to be reinfected until it is obliterated. By "dead space" we mean space that has been produced by a disease process which was not there before. The body is full. We speak of pleural and peritoneal spaces. They are potential in that they are occupied or not, as physiological processes require them. Here is a space that was formerly occupied by lung; surrounding this lung was a thin pliable pleura. Now a space has been created which is surrounded by a thick scar, sometimes a half an inch thick, and we have seen them as much as two inches thick. Inside of this scar is an empty cavity. In it is serum, pus, or mucus, as a rule. In osteomyelitis or any chronic abscess or infected cavity, "dead space"

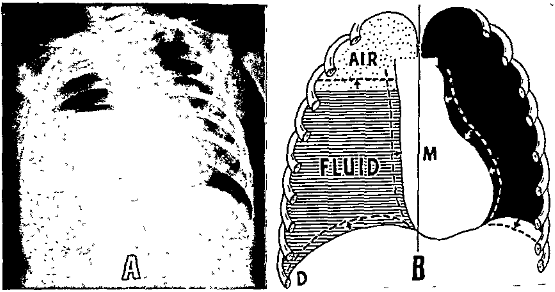


Fig. 216.—Patient in upright position. Empyema thoracis (right) after fixation. Paradoxical movement with deep inspiration; the left diaphragm descends and the left mediastinal shadow moves mesially. The right diaphragm ascends and the fluid level moves upward. *A*. X-ray photograph. *B*. Diagram illustrating movement. (*From* Berman, J. K: Surg., Gynec. & Obst. 76: 183, 1943.)

will exist unless the cavity is obliterated. In the chest it might be termed an inflammatory cyst. Such cavities or spaces are "dead" insofar as any normal function is concerned. Nature will not tolerate an empty space; it fills up with something. If sterile, it will fill with plasma from which serum exudes, thus forming an inflammatory cyst. If infected, it will fill with pus which may become sterile or be reinfected. Such spaces may be filled with air as seen in the brain (aerocele) or pleura, but the space does not remain empty. It has to fill with granulation tissue and turn into scar tissue, or it fills up with an exudate or a transudate. This is the reason for decortication operations in chronic empyema. The cavity is unroofed, and muscle and skin are transplanted to fill the void.

We shall discuss chronic empyema later. However, it should be added now that another cause for the persistence of a cavity is pulmonary

ment. The practical importance of this is obvious, for a patient can tolerate thoracic section in direct proportion to his vital capacity. If the mediastinum is not stabilized by adhesions, the normal lung suffers as much as the collapsed one. Furthermore, "mediastinal flutter" may compromise the circulation through the large venous trunks and the right auricle and may cause a kinking of the inferior vena cava as it passes through the diaphragm. The latter would be more apt to occur in right-sided empyema. But after localization occurs, so far as the thoracic mechanics are concerned, the empyema is a walled-in abscess and even with atmospheric pressure (760 mm. Hg or 14.7 pounds to the square inch) no harm occurs to the lungs or mediastinum. And, of course, as soon as the tube is removed, the opening immediately decreases in size until it is smaller than the main bronchus and negative pressure begins.

This walling in also implies that immunological localization has taken place. According to Thorsness and Higgins, this occurs for colloids after the first day and for crystalloids after the sixth day. By injecting aleuronat into the pleural cavity, this localizing process was well demonstrated by them. It is no doubt due to the formation of a pyogenic membrane with fibrin and clot occlusion of the lymphatics and later of the capillaries. An empyema, after localization has occurred, may be regarded as an abscess of the pleural cavity. If this is true, it should be treated as such. The next problem, then, was to evolve a method whereby one could find the proper time for surgical intervention by open drainage, for it was our belief that as soon as localiza*tion had occurred, operation was indicated, regardless of the consistency* of the pus or any other consideration than the ability of the patient to withstand surgical procedure.

Fraser's method for determining localization is not suitable for routine use and therefore a more practical way had to be found. We decided to use the fluoroscope as an aid. First, we observed normal subjects and we found that the mediastinal shadow is narrowed during inspiration and widened during expiration. The diaphragm descends during inspiration and ascends during expiration. With fluid, even though the mediastinum is pushed over and the diaphragm is down, there is still movement, as previously described, before walling-in occurs. However, *after localization* there is very little or no movement of the mediastinum, diaphragm, or compressed lung margin on the affected side and increased movement on the normal side. Using this method to determine the proper time for surgery, we have operated upon our patients as soon as fixation occurs. Fluoroscopic examination is made on all patients upon admission and then every other day until surgery is indicated. Other criteria such as height of fever, dyspnea, displacement of mediastinum, etc., are also used.

After localization, the second most important consideration in the treatment of an abscess is adequate drainage. In septicemia, if an acute focus can be removed or drained (all things being favorable), the patient

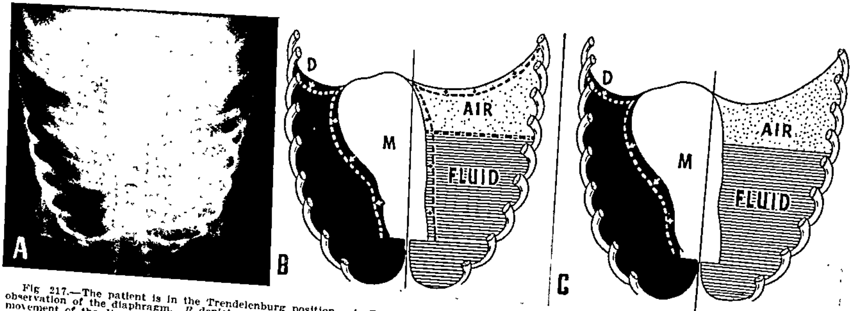


Fig. 217.—The patient is in the Trendelenburg position. *A*. Posteroanterior x-ray photograph. *B* and *C*. Diagrams illustrating fluoroscopic observation of the diaphragm. *B* depicts movement of the diaphragm cephalad (arrows) during expiration; air space decreased. It is the movement of the diaphragm that is observed. *C* shows fixation of the diaphragm. Note the band of adhesion to the diaphragm in the roentgenogram. (From Berman, J. K.: Surg., Gynec. & Obst. 76: 183, 1943.)

quired but always as infrequently as possible, for we believe with Paracelsus that "nature and not the surgeon heals wounds." We felt, too, that the tube acts as a foreign body and would actually perpetuate a cavity if left in too long. Therefore, after the seventh day the silkworm-gut suture is cut and the tube is allowed to "work its way out." This occurs due to rapid filling in of granulation tissue and some lung expansion.

If the tube is not out by the tenth day, a fluoroscopic examination is made. This will disclose fluid levels, or "pockets" with fluid, if any are present. By gently moving the patient, as *he stands upright behind the* fluoroscope, the fluid is clearly seen to move about due to the presence of air. If no fluid is present and if the drainage is thin, the tube is promptly removed. It should be remembered that the time required for the *obliteration of an empyema cavity may be exceedingly variable.* One cannot be dogmatic about the length of time that drainage should be continued. This depends upon the fluoroscopic examination and the character of the pus.

In treating our empyema cases we do not forget the patient as a whole. We have found adequate fluid intake and blood transfusions very helpful allies.

The surgical treatment of empyema is never an emergency, and in the case of streptococcic empyema, a long time is required for walling-in. Since most empyemas occur in children, we recently studied the problem and published a review describing the method of treatment which we have found successful. The treatment does not differ in adults. It should be said, however, that some authorities do not accept the "open" method of treatment (rib resection, or the removal of a small section of the sixth or seventh rib in the posterior axillary line), preferring the "closed" method, which consists of inserting a small catheter through a trocar introduced in the intercostal space. The trocar is re*moved and the catheter "sealed" in position by collodion. Some attach* a suction apparatus to the tube; others wash it at frequent intervals, aspirating the pus and then clamping again. The purpose is to maintain a negative pressure. Some authors advise repeated aspirations instead. It is perhaps better to wait for localization as determined by fluoroscopy and the character of the pus, then perform a thoracostomy by rib resection and introduce a large tube. No irrigations are done and the tube is removed in about two weeks. Breathing exercises are important if complications are to be avoided. These are outlined by Harken as originally described by Edwards. They are based on the idea that pressure over the lower and upper ribs, abdomen, and back (with the aid of a band) used successively will establish an afferent pathway whereby the patient can become conscious of the area during inspiration. During expiration the pressure *should be firmer and aids in expiration.*

No matter which method is employed in the treatment of empyema, a fundamental maxim is *the earlier the diagnosis, the sooner fluid may be*

probably will recover. Such is usually the case in metapneumonic empyema. Obviously, if a pneumonia is present (as in the synpneumonic form), the acute focus is in the lung, but if localization of the empyema has occurred, adequate drainage is indicated.

An abscess cavity properly drained must also be kept free of foreign bodies. This is done at the time of operation and any fibrinous masses which may form, later plugging the tube, are removed from it by forceps. The next step in the treatment of an abscess is obliteration of the dead space, to permit "healing from the bottom up." In empyema, healing takes place by granulations from the visceral pleura, which fuses with the parietal pleura, and by the ascent of the diaphragm. The lung expands because of (1) the contractile force of adhesions which pull it out, (2) positive pressure within the collapsed lung, because of air driven into it by forced expiration from the normal side, (3) the stretching effect of forced inspiration on the adhesions of the parietal pleura, which tend to inhibit expansion, and (4) negative pressure in the empyema cavity during inspiration, when the drainage opening is smaller than the main bronchus.

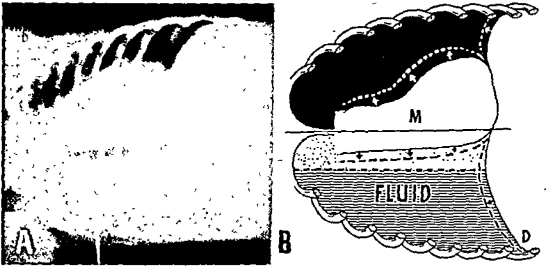


Fig. 218.—Empyema thoracis (right) observed with patient in lateral decubitus position. *A*. Roentgenogram showing the fluid level after aspiration and injection of air. *B*. Illustration depicting the movement of the diaphragm and mediastinum. With expiration the diaphragm moves upward and the mediastinal shadow widens (see arrows). The air space is narrowed. It is the movement of the mediastinal shadow that is observed. After fixation there is no mediastinal movement on the affected side.

Although massive empyema is uncommon now, the methods herein described are useful in determining the condition of the thorax, the amount of fluid, and the size of the cavity in empyemas and effusions of various types. Therefore, the maneuvers are those that will be very helpful in the diagnosis and treatment of various types of fluid accumulations. (From Berman, J. K.: Surg., Gynec. & Obst. 76: 183, 1943.)

If an abscess is to heal, the part must be put at rest and given a chance. Our study shows that prior to 1935, 77.2 per cent of these patients received daily irrigations with various solutions. Two nurses on Ward B of the Riley Hospital were kept busy giving this treatment. We have now discontinued all irrigations. Dressings are changed as re-

removed, and the sooner it is removed, the less the chance for complications or sequelae. It follows that in all types of empyema aspiration should be done first and may be continued if the amount decreases and the consistency remains thin. If purulent exudates are present, open drainage should be instituted unless the exudate may be removed as in fibrinous hemothorax (secondarily infected), where thoracotomy followed by closed drainage is indicated. Frequent fluoroscopic examinations are indispensable.

Complications and Sequelae.—Complications and sequelae result from: (1) Incomplete evacuation due to the following: (a) the disease was unrecognized and not treated. The empyema was walled in and remained as a cavity filled with serum or pus. (b) The disease was recognized

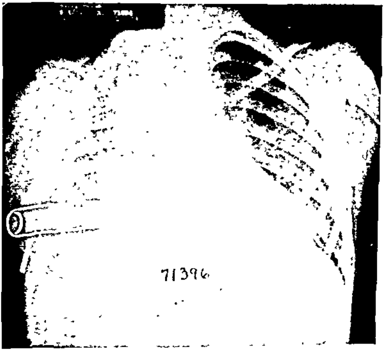


Fig. 219.—Empyema thoracis showing the tube in place after rib resection. The lung has collapsed. The chest is filled with air and a small amount of fluid. X-ray photograph retouched. This variety of empyema is uncommon now since the advent of antibiotic and chemotherapeutic agents.

and treated with a tube which was too small as in closed drainage methods, a tube large enough but removed too early, a tube improperly placed, allowing a pool of pus at the bottom of the cavity; encapsulated pockets were unrecognized at the time of operation and left behind; a foreign body may have been left, such as a piece of tubing, safety pin, piece of rib; persistent atelectasis due to the pressure of residual empyema or pain with incomplete expansion of the affected side. (c) Nature attempts to obliterate the cavity left by the disease by spontaneous drainage as in bronchopleural fistula by increased thickening of the pleura or by adhesions between visceral and parietal pleura even at the expense of pulling the labile mediastinum over or the chest wall in. Sometimes a classical deformity

Interlobar empyema is becoming more common along with many bizarre types which localize in unusual situations such as the apex and vertebral gutter. Diagnosis is usually not difficult, although lung abscess may resemble it and indeed may often be the forerunner of an interlobar accumulation. Thoracentesis, in addition to fluoroscopic examination as previously described, will usually reveal the diagnosis. Treatment by aspiration is often successful; the injection of penicillin is helpful.

Bilateral empyema is rare but requires early treatment, particularly in children whose vital capacity may be reduced to a critial level quickly. The diagnosis is made as in other types. Early aspiration is done and continued with the use of penicillin on one side at a time. Should open drainage be necessary, this may be safely done after localization.

Fig. 220 —Localized empyema. Interlobar empyema in fissure between middle and lower lobes at the level of the fifth rib. This is the type of empyema which is encountered more commonly at present, no doubt due to the effects of antibiotics and chemotherapeutic agents. *A*. Posteroanterior x-ray photograph. *B*. Lateral view.

Putrid empyema gets its name from the character of the pus which is malodorous due to the mixed flora of aerobes and anaerobes—chiefly the latter. Fusiform bacilli, spirochetes, and anaerobic streptococci are the chief offenders in the latter group. Putrid empyema is usually secondary to pulmonary abscess but is sometimes seen secondary to bronchiectasis and suppurative pneumonia. Other causes are perforation of esophagus, contamination of the pleural cavity following lobectomy, pneumonectomy or drainage of the pulmonary abscess, penetrating wounds of the thorax and mediastinum, gangrene of lung, and necrotizing pneumonitis. The symptoms and signs resemble those of other forms of empyema but

necessitatis, or bronchopleural fistula, it is enlarged. The cavity is explored, the visceral pleura removed insofar as possible or "criss-crossed" by incisions to let the lung expand if it will, and the parietal thickened pleura removed; adjacent ribs are also removed subperiostealy to give a bevelled rather than a sharp edge. If foreign bodies are present they are removed and secondary cavities are opened and unroofed. If the cavity is large, this operation must be done in stages because the patient will not stand the complete procedure in one stage. Furthermore, due to the presence of large numbers of microorganisms in the poorly drained cavity, any type of closure is apt to fail. Therefore, the unroofing is done in stages, and then three to four weeks later the closure is effected. This is more important in chronic tuberculous empyema, where the closure should not be done as long as tubercle bacilli are present, than in the nontuberculous variety. Closure is done as follows: The saucerized wound is held open and bronchopleural fistulae are closed by muscle flaps. Since proper cardiac and respiratory function are not possible without a rigid chest wall, the defect must be closed with firm tissue. Bone and cartilage would be best, but since these cannot be used, whole thick muscle transplants are employed—anteriorly the pectorals, laterally the pectoralis major, latissimus dorsi, and serratus anterior, and posterolaterally the sacrospinalis, latissimus, trapezius, supra- and infraspinatus, teres major, and minor. The muscles are sutured to the remaining visceral pleura. Then the skin is closed *loosely* over the defect, leaving a one-half inch gap. No drains or packing is used. A pressure bandage is applied.

The old Délorme operation was a decortication of the visceral pleura. Recently it has been used successfully in acute posttraumatic empyema and fibrinous hemothorax as previously described in this chapter. To peel the thick adherent visceral pleura off the lung in chronic empyema is difficult without tearing the lung with the danger of severe bleeding, bronchopleural fistulas, air embolism, and forbidding shock. The operation therefore is used only in selected cases in chronic empyema. Partial removal of this layer by light scraping may make it thinner, or criss-crossing may help by permitting some re-expansion of the underlying lung.

The treatment of lung complications associated with chronic empyema include lung exercises as described and may demand segmental resection if chronic abscess or bronchiectasis results.

Special Types of Empyema.—Although special types of empyema require recognition for proper treatment, their management does not differ greatly from the general treatment of empyema. The more common varieties which require special considerations are (1) interlobar empyema, (2) bilateral empyema, (3) putrid empyema, (4) tuberculous empyema.

Interlobar empyema is becoming more common along with many bizarre types which localize in unusual situations such as the apex and vertebral gutter. Diagnosis is usually not difficult, although lung abscess may resemble it and indeed may often be the forerunner of an interlobar accumulation. Thoracentesis, in addition to fluoroscopic examination as previously described, will usually reveal the diagnosis. Treatment by aspiration is often successful; the injection of penicillin is helpful.

Bilateral empyema is rare but requires early treatment, particularly in children whose vital capacity may be reduced to a critial level quickly. The diagnosis is made as in other types. Early aspiration is done and continued with the use of penicillin on one side at a time. Should open drainage be necessary, this may be safely done after localization.

Fig. 226.—Localized empyema. Interlobar empyema in fissure between middle and lower lobes at the level of the fifth rib. This is the type of empyema which is encountered more commonly at present, no doubt due to the effects of antibiotics and chemotherapeutic agents. *A.* Posteroanterior x-ray photograph. *B.* Lateral view.

Putrid empyema gets its name from the character of the pus which is malodorous due to the mixed flora of aerobes and anaerobes—chiefly the latter. Fusiform bacilli, spirochetes, and anaerobic streptococci are the chief offenders in the latter group. Putrid empyema is usually secondary to pulmonary abscess but is sometimes seen secondary to bronchiectasis and suppurative pneumonia. Other causes are perforation of esophagus, contamination of the pleural cavity following lobectomy, pneumonectomy or drainage of the pulmonary abscess, penetrating wounds of the thorax and mediastinum, gangrene of lung, and necrotizing pneumonitis. The symptoms and signs resemble those of other forms of empyema but

usually there is an associated productive cough with foul sputum due to lung abscess or bronchiectasis. If a general empyema instead of a localized type develops, the cough may cease but all other symptoms are aggravated. In those cases with little cough the symptoms resemble those of pneumonia. The diagnosis is made as in other forms of empyema and is definitely established by the aspiration of foul pus. *Early open drainage* is imperative. This is possible because of extensive adhesions and fixation of the mediastinum and diaphragm and is necessary because the bacteria are anaerobes and, if left in situ, will necrotize the adhesions and cause a widespread dissemination of the infection, including a cellulitis of the chest wall at the sites of thoracentesis. The mortality is high, up to 13 per cent in some statistics, due to the associated lesions and virulence of the organisms; another type of putrid empyema is that due to *Escherichia coli* which follows perforated appendicitis or other intra-abdominal infections or perforations with subphrenic abscess. The colon bacillus is a gas producer and may cause confusion in diagnosis. Usually bronchopleural fistula is thought of when the x-ray film is first seen. However, the history, associated disease, fluoroscopic examination (which is particularly helpful in distinguishing between supra- and subdiaphragmatic accumulations of air and fluid), and thoracentesis will make the diagnosis. Open drainage is indicated. In the anaerobic variety of putrid empyema, penicillin, streptomycin, and sulfadiazine are used. In the colon bacillus type, streptomycin is added up to 4 Gm. daily, given intramuscularly.

Tuberculous empyema has been discussed in Chapter 8 but should be considered here due to the commonness of the mixed types. Tuberculous pleural effusions are common. In fact, a clear straw-colored fluid which on microscopic examination shows only a few lymphocytes and no tubercle bacilli is often seen in the absence of any demonstrable pulmonary lesion. This fluid should be aspirated and injected into a guinea pig for diagnosis. The fluid should be aspirated at frequent intervals as previously described. *Empyema implies the active growth of tubercle bacilli* in the fluid. Three types are seen: (1) a thin cloudy fluid without pus but with demonstrable tubercle bacilli, (2) a more purulent type without pyogenic organisms, and (3) a mixed type with frank pus and pyogenic bacteria as well as tubercle bacili. In all types the primary consideration is the general care of tuberculosis by medical means. At present this includes the use of streptomycin for short periods of time. In addition, the first type may be controlled by repeated aspiration. If thoracoplasty seems indicated, it should be done. In the second type a thickened pleura may be present and thoracoplasty may not cause a collapse of the pleural cavity. Decortication may be done in early cases; however, there is danger of a mixed type of empyema. In the third or mixed type open drainage should be done promptly. Here the Eloesser flap may be used to avoid tubes (which act as foreign bodies) and yet produce prolonged drainage. This is accomplished by turning in a flap of skin

after thoracotomy and suturing it to the parietal pleura. Should a chronic empyema cavity result, as will usually occur, it should be saucerized and closed as previously described. We have recently done combined visceral and parietal decortication in several cases of this type with encouraging results. This procedure is useful in cases without active intrapulmonary disease. In the presence of active parenchymal lesions or cavities, decortication would mobilize the lung and disseminate the infection inside as well as outside the lung in the pleural cavity.

PNEUMOTHORAX

We have already considered pneumothorax under Injuries to Chest and in Chapter 8 under Tuberculosis. The term is ordinarily used to mean *intrapleural* collections of air. Extrapleural pneumothorax does occur in connection with penetrating injuries and subcutaneous emphysema, extrapleural infections with gas-producing organisms, and also as a result of the injection of air extrapleurally for therapeutic reasons in the treatment of tuberculosis. *Intrapleural* pneumothorax may be due to an open or penetrating wound, traumatic pneumothorax, or, under tension, tension pneumothorax. Spontaneous pneumothorax usually is associated with pulmonary tuberculosis, and artificial pneumothorax is used to produce a lung collapse in the treatment of the disease (see Chapter 8).

Pneumothorax may be associated with extraneous air in the tissue (interstitial emphysema, subcutaneous emphysema), in the mediastinum (mediastinal emphysema), and in the abdomen (pneumoperitoneum). Other causes for acute pneumothorax are cystic disease of the lung, emphysema, blebs due to emphysema of the "giant" variety or cysts associated with "giant" emphysema, and in the so-called "chronic" types of spontaneous pneumothorax, bands in addition to blebs cause repeated attacks. The treatment of spontaneous pneumothorax depends upon the cause. If not under tension, it is probably best left severely alone until it is absorbed; then careful x-ray and bronchoscopic studies may be done to determine the underlying lesion. If it persists, it should be aspirated and diagnosis of the morbid anatomy of the lung made. If no lung disease is found, no active treatment is instituted. In cystic disease, lobectomy or segmental resection may be necessary, whereas in emphysema, unless of the bulbous type, surgery is not necessary. Sometimes it is difficult to differentiate between a giant cyst and a spontaneous pneumothorax, especially if it is a hydropneumothorax. Aspiration under such circumstances may be unwise because of the danger of empyema. Spontaneous pneumothorax is not uncommon after major surgery in the abdomen or elsewhere. It may be very serious and result in death from anoxemia even though unilateral and almost always when bilateral in spite of any treatment.

THE LUNGS

Within the pleural cavities lie the lungs (pulmones) with which we breathe. Impure blood is brought to the right auricle by the superior vena cava (from the head and neck) and by the inferior vena cava (from the rest of the body). From here it goes

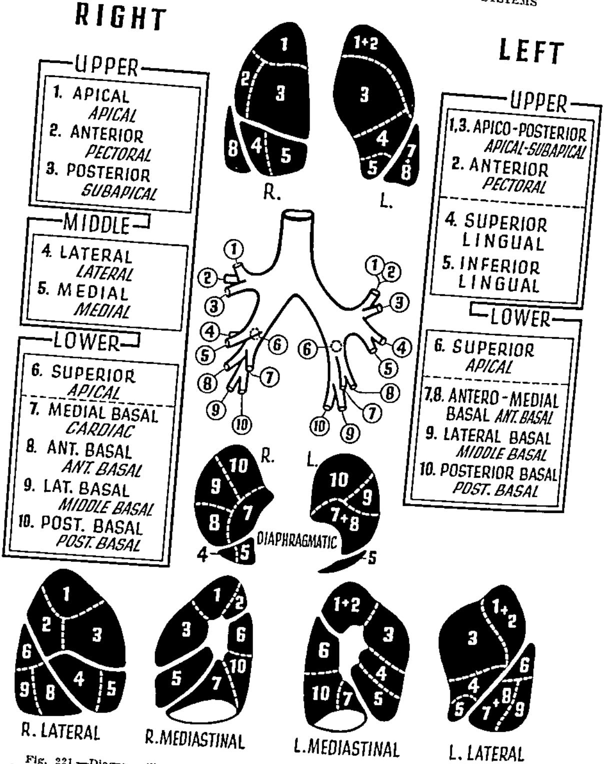


Fig. 221.—Diagram illustrating the tracheobronchial branching correlated with subdivisions of the lungs after Jackson and Huber. (Nomenclature based upon studies of Jackson, C. L., and Huber, J. F.: Correlated Applied Anatomy of the Bronchial Tree and Lungs With a System of Nomenclature Dis. Chest 9: 319, 1943; Boyden, E. A.: A Synthesis of the Prevailing Patterns of the Bronchopulmonary Segments in the Light of Their Variations, Dis. Chest 15: 657, 1949; Brock, R. C.: The Anatomy of the Bronchial Tree, London, 1946, Oxford University Press [also personal communication]; Scannell, J. G.: An Anatomic Approach to Segmental Resection, J. Thor. Surg. 18: 64, 1949.)

through the tricuspid valve to the right ventricle which pumps it to the lungs through the pulmonary artery. In the lungs the impure blood releases its carbon dioxide and takes its oxygen and then hurriedly rushes through the pulmonary vein to the left auricle, through the mitral valves to the left ventricle and out into the aorta to be carried to all parts of the body. To make this purification possible the lungs are composed of tiny air sacs (alveoli) which are made up of epithelial cells fused into thin, structureless plates of tissue. Immediately adjacent to these plates are the endothelial cells of the capillaries. In addition, there are elastic fibers which allow the alveoli to

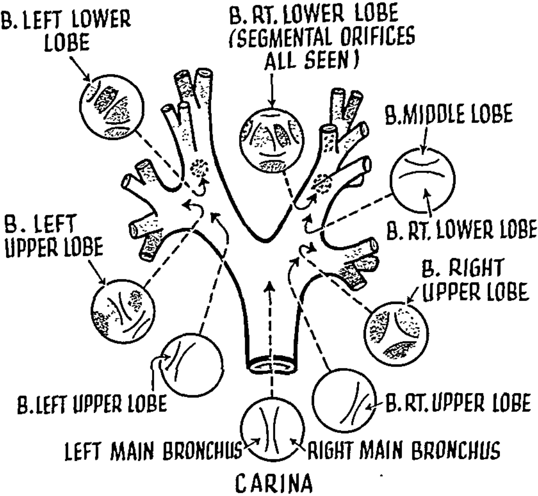


Fig. 222.—Diagram of the bronchi to the lobes and their segmented branches with endoscopic landmarks as seen through the bronchoscope when the patient is examined in the dorsal recumbent position. (Redrawn from Jackson and Huber: Correlated Applied Anatomy of the Bronchial Tree and Lungs With a System of Nomenclature, Dis. of Chest 9: 1, 1943.)

become greatly distended and some macrophage cells (dust cells) to engulf foreign bodies, such as soot, thus making the adult lung gray. Respiration takes place by the transfer of gases through the alveolar plates and endothelial cells. The alveoli are gathered about the bronchioles. These lead to the bronchi, which lead ultimately to the trachea. The entire lung is divided into lobes: three in the right and two in the left. These in turn are subdivided into segments (Fig. 221) with names as indicated by Jackson and Huber. The general scheme of division is based upon a broncho-

vascular distribution, making possible segmental resection in bronchiectasis and other diseases for which only a portion of the lobe need be removed. At surgery the lobe is deflated, the bronchus temporarily occluded and then reinflated by positive pressure through the endotracheal tube. In this manner avascular planes are found between segments, allowing for a bloodless dissection between these units. The divisions of the lung on the right are upper, middle, superior lower, and basal lower; on the left there are the upper, lingular, superior lower, and basal lower. These are subdivided into segments as shown in Fig. 221. In addition, there may be extra lobes such as the azygos lobe, caused by an abnormal position of the vein, producing a septum in the right upper lobe covered by two layers of parietal and visceral pleura because the vein is extrapleural. Another is an extra lobe in the space between the pericardium and diaphragm on the right or left side.

We have already studied the mechanics of respiration. It remains to be said that respiration is under the control of the respiratory center in the medulla. This center is affected by (1) voluntary impulses, (2) gases—carbon dioxide, and, to a lesser degree, oxygen, and (3) nervous impulses by way of the vagi and sensory nerves, which may have a pressor or depressor effect (discussion under Physiology of Respiration).

Congenital Anomalies of the Lungs

In addition to the extra lobes which are occasionally seen, there may be other anomalies. We have recently seen a case of complete agenesis of the left lung with a blind left main stem bronchus. Pericardial deficiency with bronchiogenic cyst has been called iter venosum since it is due to abnormal development of the left duct of Cuvier.

Cystic Disease of the Lungs.—Cystic disease of the lungs may be congenital or acquired. Sometimes the distinction is very difficult and cannot be made even by microscopic study. This is due to the fact that abscess cavities become epithelialized and cyst cavities become infected. In the newborn true cystic disease is suspected. Widespread cystic disease consisting of hundreds of various-sized cysts involving one or more lobes or even both lungs is practically always congenital. Other names given to cystic diseases are pulmonary cysts, bronchogenic cysts, pneumocysts, and pneumatoceles. Some authors include cystic bronchiectasis which may be present at birth or acquired later in life. However, mediastinal cysts of bronchogenic type, parasitic, hydatid cysts, tuberculous cavities or cavitary infections, or carcinoma should not be included.

True Congenital Cystic Disease.—True congenital cystic disease includes some bronchogenic or bronchoalveolar cysts. The cysts are found in the pulmonary parenchyma and sometimes are attached to the trachea or a main stem bronchus. They are lined with bronchial epithelium, but their walls contain cartilage, smooth muscle, elastic tissue, and glands in more or less disorderly arrangement. Therefore, some pathologists have called them cystic teratomas. Pulmonary abscess and simple bronchial dilatation usually have a different picture but may be similar. Clinically and pathologically, two types are seen: the large solitary cyst seen in infancy and childhood as a rule and the multiple cystic disease composed of multilocular or unilocular cysts. The latter type may be associated with polycystic disease of the kidneys and liver. Complications of congenital cystic disease include accumulations of fluid, hemorrhage,

secondary infection, hemopneumothorax, pneumothorax, empyema, acquired cysts, bronchiectasis, pneumatocele, pneumonia, and all of the other complications of chronic pulmonary suppuration.

Acquired types include pneumatoceles, which have no epithelial lining and therefore tend to disappear spontaneously, abscess cysts, emphysematous blebs, and bullae. Other cysts include bronchogenic cysts and pulmonary cysts resulting from infection, penetrating wounds, hemorrhage and noxious gases.

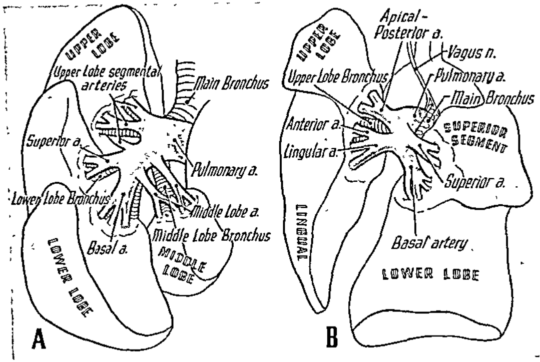


Fig. 223.—Diagram illustrating the pulmonary arteries with their branches. *A*, Right pulmonary artery as seen anteriorly with the lobes widely separated. The middle lobe has been rotated medially; its arteries run posterior to the bronchus although the diagrams make them appear anterior because of the retraction of the lobe. The main artery descends below the upper lobe bronchus. The first branch is usually the common stem superior pulmonary trunk which separates into the apical and anterior segmental arteries. The third artery usually supplying the upper lobe is the posterior segmental branch which arises from the inferior trunk opposite the middle lobe branches and ascends into the posterior portion of the upper lobe. The inferior pulmonary trunk is found anterior to the intermediate bronchus. The medial and lateral arteries to the middle lobe arise from the anterior aspect of the inferior trunk. Sometimes they begin as a common trunk and split into medial and lateral and often other branches. The basal branches follow the corresponding bronchi. The first branch is the superior segmental artery and it arises at the same level and posterolateral to the middle lobe branches. The arteries to the basal segments arise from the inferior pulmonary trunk independently. They are the medial, anterior, lateral, and posterior basal segmental arterial branches.

B. The left pulmonary artery lies above the left main bronchus and the superior pulmonary vein just beneath the aortic arch. This diagram shows the branches with the lobes widely separated. The artery winds around and behind the upper lobe bronchus. The first branch is the apical-posterior segmental artery which divides into an ascending or apical and posterior segmental branch. Sometimes the two branches originate independently. The next branch to the upper lobe is the anterolingular trunk which gives rise to the anterior segmental branch and the two lingular branches. The latter may come off as a common trunk and then divide, or they may come off the anterolingular trunk independently as illustrated. They supply the superior and inferior lingular bronchopulmonary segments.

Branches to the lower lobe come off the interlobar portion of the artery. The superior segmental branch arises at a higher level than the lingular arteries. It divides into two or three branches. The arteries to the basal segments lie anterolateral to the bronchi and are four in number—anterior, medial, lateral, and posterior basal. (Modified from Overholt, R. H., and Langer, L.: Surg., Gynec. & Obst. 84: 257-268, 1947.)

Diagnosis.—Diagnosis is made by the history and symptoms and signs. The latter include cough which may or may not be productive, depending upon whether or not there is a communication with a bronchus. Hemoptysis may be present. Any of the findings of chronic pulmonary disease may be present, making the differential diagnosis difficult. Such lesions as dermoid cysts or other neoplasms, abscess, localized empyema, cavitary tuberculosis, hydatid cyst, and diaphragmatic hernia must be taken into consideration. X-ray examination and bronchography with Lipiodol are of great help.

Treatment.—Treatment depends upon the type of cyst encountered. In general it is surgical and includes the complete removal of the cystic portion of the lung, conserving as much lung tisue as possible. Partial or complete lobectomy or pneumonectomy may be required. Age is no contraindication to surgery.

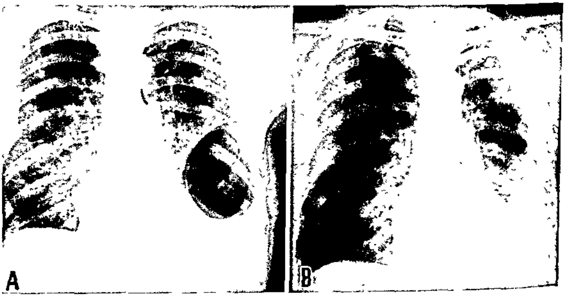


Fig. 224.—Pulmonary cyst of the lung. *A.* Pulmonary cyst of the left lower lobe. T. U. C., a man aged 50 years, first noticed symptoms after a severe blow on left chest by a falling post. These consisted of persistent cough, dyspnea, and pain in the left lower chest and left shoulder. They were thought to be due to possible rupture of smaller cysts into the larger one. The patient is emphysematous as disclosed by the decrease in peripheral markings and hyperillumination of lung fields with accentuation of the hilar markings. The differential diagnosis included bullous emphysema (pneumatocele, pneumocyst, balloon cyst) due to giant bullae formation, pneumothorax localized due to previous adhesions; congenital cystic disease because of the small cyst in the right lower lobe, and inflammatory cyst (old lung abscess which had sealed off the previously communicating bronchi with gradual absorption of retained exudate). Final diagnosis was acquired lung cyst due to lobular emphysema with check valve obstruction of the bronchial lumina. Left lower lobectomy was done. Microscopic examination showed pulmonary cyst, fibrosis, patchy pneumonitis, and anthracosis of pulmonary tissue. *B.* Postoperative film. There is still some pleural reaction in the left costophrenic angle. Patient made an uncomplicated recovery. (Case referred by Dr. R. Henry and Dr. D. Stone.)

Arteriovenous Fistula of the Lung.—Arteriovenous fistula of the lung may be congenital or acquired. The latter is rare. Congenital types are really large cavernous hemangiomas which are found anywhere in the lung and may include the mediastinnm. They lead to anoxemia with cyanosis, polycythemia, osteoarthropathy, and other symptoms, due

to the interference with respiration and poor oxygenation, because impure blood is shunted from the pulmonary arteries to the pulmonary veins. On auscultation a continuous murmur is heard. The x-ray examination shows the shadow which may be seen to pulsate under the fluoroscope. Angiography aids greatly in the diagnosis. The treatment is lobectomy or, in rare cases, pneumonectomy.

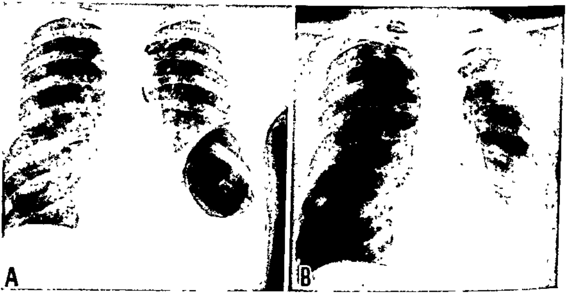
Injuries.—Injuries to the lung result from fractured ribs, punctured wounds, gunshot wounds, or blast injuries. The effects of such injuries are collapse of the lung and hemorrhage. The patient coughs up bright red blood, is dyspneic, and may go into shock. Soon the pleural cavity may fill with blood, or if the injury is less extensive, blood fills the alveolar spaces, producing consolidation with dullness, increased vocal fremitus, and tubular breathing. The treatment consists of closure of the wound at once and wiring or otherwise immobilizing rib fragments, morphine for sedation, and blood transfusion. Dyspnea is relieved by the administration of oxygen. Thoracotomy may be necessary. (See discussion under Injuries to the Chest.)

Infections of the Lung

Pneumonia.—Perhaps the most common *inflammatory* lesion is pneumonia. Pneumonia may be defined as an infectious inflammatory lesion of the lung caused by pathogenic bacteria and characterized by exudation with more or less consolidation. It may be classified as lobar, broncho pneumonia, lobular or patchy, central, interstitial, aspiration or postoperative, and hypostatic. It may be caused by the pneumococcus, streptococcus, staphylococcus, Friedlander's bacillus, *Hemophilus influenzae*, tubercle bacillus, virus, and miscellaneous infections such as influenza, tularemia, coccidioidomycosis, moniliasis, and histoplasmosis. The surgeon is particularly interested in those types of pneumonia due to aspiration, bronchial obstruction, and hypostasis. To avoid this, every provision is made for keeping the trachea and bronchi free from foreign material. The stomach is aspirated in pyloric occlusions; the esophagus is emptied in esophageal occlusions; frequent aspirations are done if there has been any vomiting. The patient is placed in the head-down position and, after all lung operations, the anesthetist sucks out the trachea through the endotracheal tube and again after its removal at the conclusion of the operation. Early mobilization, deep breathing, holding the chest and forcing the patient to cough after chest operations prevents and relieves bronchial obstruction and hypostasis. The pre- and postoperative use of the sulfonamides and penicillin also help to prevent these complications and to control pneumonia after it occurs. Oxygen is used after chest operations and others as indicated with reservations as previously outlined in this chapter. Postoperative pneumonia is more common after spinal than inhalation anesthesia. The latter does cause bronchial irritation; the former is accompanied by small emboli

Diagnosis.—Diagnosis is made by the history and symptoms and signs. The latter include cough which may or may not be productive, depending upon whether or not there is a communication with a bronchus. Hemoptysis may be present. Any of the findings of chronic pulmonary disease may be present, making the differential diagnosis difficult. Such lesions as dermoid cysts or other neoplasms, abscess, localized empyema, cavitary tuberculosis, hydatid cyst, and diaphragmatic hernia must be taken into consideration. X-ray examination and bronchography with Lipiodol are of great help.

Treatment.—Treatment depends upon the type of cyst encountered. In general it is surgical and includes the complete removal of the cystic portion of the lung, conserving as much lung tisue as possible. Partial or complete lobectomy or pneumonectomy may be required. Age is no contraindication to surgery.



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(1) penetration from outside; (2) blood stream infections (septicopyemias) and phlebothrombosis, which rarely causes a pulmonary abscess in our experience; (3) aspiration, such as foreign bodies spill from esophageal obstruction, etc., (4) extension from subphrenic or perinephric or retropharyngeal abscess. The causative organisms are variable, including aerobes and anaerobes, pneumococci, staphylococci, fusiform bacilli, hemolytic streptococci, *Micrococcus catarrhalis*, spirochetes and many others.

Pathology.—The pathology varies with the cause and the organisms found. Abscesses may be single or multiple, unilateral or bilateral, in the upper or lower lobe (about equal), and if in the lower, it is in the posterior basal or apical portion. Every lung abscess begins with a localized pneumonitis which is often thought to be a lobar pneumonia. The mechanism of infection is due to an obstruction of the bronchus or bronchiole in aspiration types (putrid abscess) or by embolism, in which the pulmonary artery branches are obstructed. In either instance we note the element of obstruction first. In the former, atelectasis results which makes the area suitable soil for bacterial growth because of interference with the blood supply; in the latter, infarction results from vascular occlusion and local anoxemia and then the infection begins. We have seen that the lobes of lungs are divided into bronchovascular segments. It is in the periphery of these segments that abscess is most apt to occur. The so-called central abscess may appear to be central but is usually at the periphery of a segment or facing a fissure, the diaphragm, mediastinum, or pericardium. This is important because if true, abscesses will be peripheral with only a little margin of lung between them and the pleura; moreover, there will be early adhesions between the visceral and parietal pleura. The reaction of the tissue to the bronchial or vascular insult will result in (1) no infection or, if infection occurs, resolution may and does occur; (2) necrosis with absorption as in infections elsewhere; (3) necrosis with sloughing; or (4) suppuration which may occur within two weeks from the time of onset. After about six weeks, other lesions may appear; secondary abscess, multilocularity, due to spilling over into adjacent bronchi or through intercommunicating bronchi, spread of infection peripherally along bronchovascular segment, interstitial pneumonitis, fibrosis and bronchiectasis, epithelialization, hemorrhage, rupture of the abscess with empyema, bronchopleural fistula, involvement of surrounding lung with thickening and fibrosis of septa and complete obliteration of alveoli, and metastatic abscess in the skin, kidneys, spleen, and, rather commonly, in the brain. The abscess may be simple (early) or complicated (late). Very late there may be clubbing of the fingers and amyloid disease. The abscess may break into an open bronchus or bronchi and be coughed up, or it may rupture into the pleural cavity; in either instance the abscess may then heal, but in the latter a residual empyema may remain.

with pneumonia. Bronchial irritation and occlusion with mucous plugs is a common cause of pneumonia and atelectasis. The pernicious habit of keeping patients so narcotized that their respirations are shallow and they are immobile for long periods of time is perhaps the greatest cause of this complication.

Lipoid Pneumonia.—Lipoid pneumonia occurs after fractures of the long bones, due to fat emboli. Recently some have thought that it may occur as a result of the use of oil in the nose, or even in the eyes, through aspirations of the fatty droplets.

Above all, the old debilitated patient is a ready host for bacteria due to his weakened resistance, and he must be watched carefully and moved early. The surgeon is called upon not infrequently to care for lung abscess and empyema following pneumonia.

Pulmonary Abscess and Gangrene.—Lung tissue may be infected by many organisms and reacts in many different ways. What might be said to be a general infection of the lung is seen in pneumonia. The local type of infection, which may follow, is seen in abscess and gangrene.

Etiology.—Experimentally it is difficult to produce an abscess by the injection of infected material into the bronchial tree because of the cough reflex and the normal action of the cilia. If the bronchus is blocked by a foreign body or if infected emboli are used, abscess results. The cause of lung abscess is not clearly understood; perhaps it is better to say there are probably many causes. A lung abscess may occur after an acute upper respiratory infection or pneumonia but is more commonly seen postoperatively. In general, the infection has two ways of entering. The first is by the bronchial tree. After operations done under general anesthesia, infected mucus or blood is aspirated and even bits of tonsil or other tissue may lodge in a bronchiole. This produces an atelectasis of a small lobule or lobe, with subsequent infection. (Closure of the outlet traps virulent bacteria.) This type sets up a gangrenous bronchopneumonia of the bronchopulmonary segment with liquefaction and abscess formation. Since we see this condition after operations other than those performed on the nose or throat, and when local or spinal anesthesia has been used, we must assume that the second way infection enters the lung is by embolism (see Chapter 17). In either case, an area of infarction ensues, with destruction of lung tissue and subsequent suppuration. The history is usually typical. An operation was performed a week before; then the patient developed a dry cough. There was fever, which became septic in type. Soon the cough became productive, with foul-smelling sputum. Then there was dullness on percussion and râles were heard.

Other causes for abscess are foreign bodies, subphrenic abscess, congenital cystic disease, penetrating wounds, retropharyngeal abscess, spillover from esophageal obstruction due to carcinoma, diverticulum, or achlasia. In general, the causes may be summarized into four avenues:

chronic types it may help in the differential diagnosis between bronchogenic carcinoma, lung cyst which is secondarily infected, bronchiectatic cavity, localized empyema, interlobar empyema, and tuberculosis. Repeated sputum examinations and thoracentesis may aid in the diagnosis. Fluid levels on x-ray examination are seen in only one-half of the cases. The presence of multiple types of lesions is an ever-present possibility; abscess with carcinoma (about 5 per cent in our cases) or with tuberculosis is not uncommon. Carcinoma and abscess are common enough to warrant comment. The combination may be due to the carcinoma itself which is secondarily infected or due to the obstruction of bronchi by the growth causing abscesses distally; if the neoplasm is in the upper lobe, there may be spill over with subsequent abscess in the lower lobes.

Treatment.—Prophylactic treatment includes care of the mouth prior to any elective surgery but no radical "clean up" which may disseminate infection. The anesthetic and early postoperative periods are important in the prevention of lung abscess. Vomiting with aspiration of food particles, if the patient has some type of gastric obstruction, may be prevented by gastric aspiration. This is done routinely in pyloric obstruction from any cause not only because of vomiting but because decompression is necessary for successful surgery. Emesis of liquids may be equally disastrous if aspirated. Foreign bodies such as teeth, bits of tonsil, blood, and mucus may act as the nidus for an abscess. The same factors are true during the early postoperative periods. Here deep breaths and encouragement to cough are most important. If coughing is too painful, enough sedation is used to make it possible or the pharynx and upper trachea are aspirated with a catheter attached to a suction machine. Aspiration by bronchoscopy should be done after long deep anesthesia and thoracic operations where endotracheal anesthesia has been used. Strong sedatives and narcotics are used sparingly. The patient is mobilized early and encouraged to cough.

Medical treatment should be given a trial for six to eight weeks. Sulfadiazine in large doses, penicillin intramuscularly, 100,000 units every three hours, streptomycin, 0.25 Gm. every six hours, and postural drainage and bronchoscopic aspiration should be given a trial.

Later, after adhesions have formed (three to four weeks), the abscess cavity may be aspirated and pencillin with streptomycin injected. This will be coughed up as a rule because there are usually two to three bronchi which open into the cavity. Bronchoscopy is very helpful and is imperative if a foreign body is suspected. It should be given a trial.

Surgical treatment consists of drainage of the abscess cavity or removal of the affected lung segments. If medical treatment fails after six to eight weeks, thoracostomy may be done. We do not use the two-stage operation because adhesions are present early between the visceral or parietal pleura and the two-stage operation cripples the lung unnecessarily. The abscess having been located by x-ray, one or two rib sections

Symptoms and Signs.—The earliest and most persistent symptom is cough, unproductive at first, then odorless sputum, and finally foul sputum. Hemoptysis in about one-half the cases, chills and fever, rapid weight loss, dullness on percussion, suppressed breath sounds, and râles

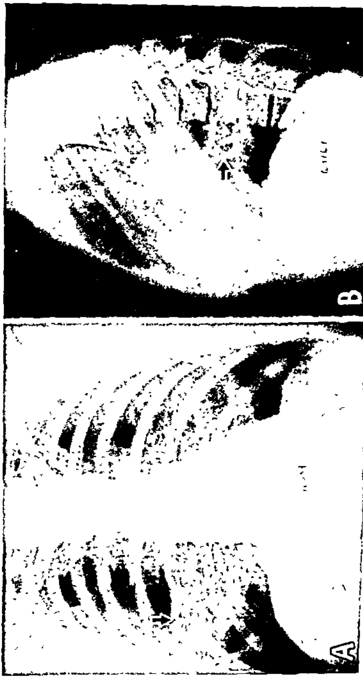

Fig. 225.—*A*, Lung abscess, right middle lobe. There is thickening of the interlobar pleura between the middle and the upper lobe. A fluid level may be seen in the abscess cavity, which is surrounded by a rather large inflammatory zone. *B*, Lateral view. The arrow points to the abscess cavity. Lobectomy of right middle lobe was done.

over the abscess area are present. X-ray examination (posterioranterior, lateral, and oblique films) is necessary for diagnosis and exact location of the abscess. Bronchoscopic examination is helpful but bronchography with Lipiodol is useless in the acute phase because it will not enter the cavity because of bronchiolar obstruction and may be dangerous. In the

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are removed, and if adhesions are found, aspiration is done, and then the abscess cavity is opened and drained with soft rubber dam tissue. If the abscess is not adherent as in the interlobar type, the normal lung may be sutured to the parietal pleura, then aspirated, and a small Penrose drain inserted. The two greatest dangers from open drainage are hemorrhage and brain abscess due to septic emboli. Some will not heal and the remaining abscess must be removed with the lung segment. Such cavities are usually lined with epithelium. Sometimes the cavity may be closed by muscle flap transplants. Open drainage is not often employed by us except when associated with empyema.

Complicated (multiple abscess, bronchiectasis) and late abscess cavities will not heal by open drainage in most cases. For these we use segmental resection or lobectomy. If multiple and disseminated abscesses are present, pneumonectomy may be necessary to effect a cure. Following lobectomy, closed drainage is employed anteriorly and posteriorly.

Abscess with empyema requires open drainage and additional opening of the abscess cavity so that it will drain properly. Thus the abscess and bronchopleural fistula will fill in as the empyema heals. Chronic empyema is treated by the Schede thoracoplasty with closure of the cavity by muscle flaps from the pectoralis anteriorly in upper lobe cavities, latissimus in lower lobe and sacrospinalis in paravertebral cavities. By this method the decortication is held to a minimum and the bronchopleural fistula will close. We recently reviewed 28 cases of lung abscess which we treated in the following ways: (1) medically with the aid of bronchoscopic aspiration. Two cases, both recovered. (2) Aspiration without injection of penicillin or streptomycin into the cavity, but with their aid intramuscularly. Two cases, both recovered. (3) Open drainage, seven cases. Two were chronic and complicated by localized empyema. They recovered. One was chronic and uncomplicated (cystic type). This patient recovered but returned nine weeks later with a brain abscess and died. One man was dismissed from the hospital and later had an exsanguinating hemorrhage from the drainage site and by hemoptysis. Two cases later required lobectomy. (4) Lobectomy. Fifteen cases. One was an acute complicated type with gangrene. (This followed an anesthetic given during childbirth in a primipara aged 41 years. A tooth broke off and was aspirated.) Two cases subsequently developed empyema with bronchopleural fistula and were treated by open drainage. (5) Lobectomy and pneumonectomy. Two children. One had a lower lobectomy and then developed bronchiectasis in the upper lobes and was subjected to pneumonectomy on the operated (right) side. The other had the primary abscess in the lingula with secondary abscess in the upper lobe and bronchiectasis in the lower. Pneumonectomy was done. Both recovered. Thus in our limited group of recent cases, 61 per cent ultimately required lobectomy or pneumonectomy. Al-

most 50 per cent of all open drainage cases later required lobectomy. Late cases with localized empyema responded well to open drainage.

Pulmonary Tuberculosis.—Pulmonary tuberculosis is discussed in Chapter 8. Since the disease may require lobectomy or even pneumonectomy, the indications for these procedures should be enumerated. They are as follows: (1) bronchial stenosis, especially with febrile attacks and positive sputum from this area, if the remainder of the lung is quiescent. (2) Areas of tuberculous bronchiectasis. (3) Hemorrhages from bronchiectatic area. (4) Atelectatic lobes. (5) Cavities that persist in spite of pneumothorax although thoracoplasty in the upper lobe may be tried first. (6) Tuberculosis confined to the lower or middle lobe when,

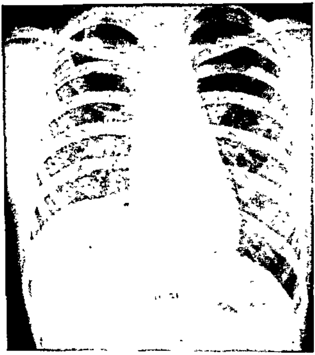

Fig. 226.—Paralysis of the diaphragm on the right, due to phrenectomy. The diaphragm is in the position of extreme expiration.

because of adhesions, pneumothorax or phreniclasia does not control it. (7) Solitary large tuberculomas which will cause dissemination, if not removed. (8) Massive tuberculosis in one lung which has been considered by some to be an indication for pneumonectomy—this is doubtful. (9) In the young if thoracoplasty is indicated, lobectomy may be preferable because it obviates the resultant scoliosis. (10) In chronic case with limited disease that does not respond to other forms of treatment yet does not spread.

In addition to lobectomy, the general treatment of tuberculosis should be carried out because the removal of a focus does not mean that the disease is entirely arrested.

Massive Collapse.—Massive collapse of the lungs occurs as a result of the obstruction of a bronchus by a plug of mucus and subsequent absorption of the air trapped in the obstructed alveoli, with resulting atelectasis. Massive collapse occurs more frequently after gas anesthetics. These are quickly absorbed from the alveoli. It is more common after spinal anesthesia than after inhalation anesthesia. Prolonged anesthesia of any kind increases the chance for accumulation of secretion. Therefore, light anesthesia which is stopped as soon as possible is best. The incidence is higher in men, in smokers, after surgery in the upper abdomen, in patients with acute or chronic respiratory infections, in the old, and in patients undergoing long operations. This is due to a sharp

Fig. 227.—Massive collapse of the lung (right). Note the mediastinal shifting toward the affected side, the narrowing of the intercostal spaces, and the diminished aeration on this side.

reduction in vital capacities, a decrease in subtidal volume of the lungs, and decreased excursion of the diaphragm. In the presence of an obstructed bronchus, atelectasis quickly occurs. Pneumonia, lung abscess, or fibrosis may follow massive collapse. This is not uncommon postoperatively in the small bronchioles; obstruction of the large bronchi is less common and produces the most marked symptoms. The clinical picture is one of pneumonia. There is rapid distressing respiration, with pain and cough. Some cyanosis exists and the temperature rises to about 101 to 102° F. The condition is distinguished from pneumonia by the distant breath sounds and by the displacement of the heart and mediastinum *toward the affected side.* A bedside roentgenogram clinches the diagnosis, in massive cases, not in lobar or lobular types. If fever and toxemia continue, it is probably bronchopneumonia.

Prevention.—Heavy smokers are asked to stop for one week prior to surgery, and all patients with chronic respiratory irritation are asked to cough before anesthesia is given. Atropine as a preanesthetic agent helps. The anesthetist may hyperventilate the lung with carbon dioxide and oxygen during the surgery; however, this does not always prevent the complication. The patient after operation must move about frequently and be forced to take deep breaths. The best time to encourage this is immediately after morphine has been administered, for there is no doubt that shallow respiration results from pain and not from reflex paralysis of the diaphragm, although the latter may play a secondary role. While it is true that morphine depresses the respiration, it also relieves pain and thereby makes deep breathing and early motion possible. The *treatment* of massive collapse after it has occurred is also deep breathing, early mobilization, and holding the patient's affected side to help cough up the plug of mucus. Inhalation of 5 to 10 per cent carbon dioxide stimulates deep breathing and is sometimes effective. The bronchoscope may be passed in rare cases. Sulfadiazine and penicillin are given to reduce infection. The prognosis is good.

Pulmonary Embolism.—Pulmonary embolism has been mentioned in Chapters 6 and 17. As was pointed out then, pieces of thrombi or fat or air bubbles may be carried to the pulmonary vessels. By far the most common are bits of thrombi, which, if small, produce infarcts, and, if large enough, completely occlude the pulmonary artery, causing an entire lobe, or even lung, to be deprived of blood and, because of the sudden onset, resulting in death from asphyxia. The condition usually occurs seven to ten days after operation and manifests itself by pain and cough, with blood-tinged sputum. Local signs of dullness, friction rub, and harsh sounds may be elicited. Sometimes the patient is cyanotic and dyspneic. The outcome of an embolism depends on its extent and infectivity; usually it ends in resolution. Sometimes pneumonia, pulmonary abscess, empyema, and even death may occur. Often successive emboli occur, singly or in showers. The *treatment* consists primarily in prevention. This is discussed under phlebothrombosis and thrombophlebitis (see Chapter 17). Deep breathing exercises, turning of the patient, early mobilization in old people, and adequate intake of fluid all are designed to prevent thrombosis, which may presage embolism. The surgeon must handle tissues gently, especially where large plexuses of veins are present. Should embolism occur, the treatment resolves itself into treating whatever effect the embolism has produced (q.v.). The Trendelenburg operation which consists of pulmonary arterial embolectomy has occasionally been done with success.

Pulmonary embolism has long been recognized as a surgical complication. Recently its importance in medical patients has led to early ambulation in heart and other medical diseases. Air embolism is rarely due to intravenous medication since 5 to 10 c.c. have been injected rapidly in man without producing clinical symptoms. A gaping wound in

a large vein (internal and external jugular or axillary) with fixed facial coverings preventing collapse may cause fatal pulmonary embolism. Entrance of air into the pulmonary vein following pleural punctures, pneumothorax, or operations on the lung causes obstruction of the arterial tree. Should air embolism occur, 100 per cent oxygen is administered. While the cause is controlled, rarely the knee-chest position following delivery, tubal insufflation, or the injection of air about the adrenals for diagnosis may cause air embolism.

Fig. 228.—Lung with multiple areas of infarction. Arrows point to three such wedge-shaped areas. Post-mortem specimen.

Nontuberculous Infections of the Lungs

Actinomycosis.—Actinomycosis has been discussed in Chapter 7. The pulmonary form is probably secondary to aspiration from the mouth. The diagnosis can only be established by finding actinomycotic granules in the excised tissue from draining sinuses or persistently in the sputum.

Encouraging reports have been given from the treatment of the disease by sulfadiazine, penicillin, lobectomy, and pneumonectomy.

Coccidioides Immitis.—*Coccidioides immitis* may produce an infectious granuloma in the lung following the inhalation of infected dust. The infection is usually mild, involves the lungs and mediastinal nodes, and soon disappears, leaving a scar. Exceptionally an abscess may form which may break into a bronchus or cause secondary lesions. Rarely the infection gains entrance into the blood stream causing death. The differential diagnosis includes tuberculosis, residual pneumonitis, fibrosis, healed abscess, bronchitis, bronchiectasis, Boeck's sarcoid, and metastatic carcinoma or sarcoma. Skin tests with coccidioidin study of the sputum and blood help in the diagnosis. There is no specific treatment although chemotherapy and antibiotics may be used.

Histoplasmosis.—Histoplasmosis in the lungs is far more common than was formerly believed. Furthermore, it is not always fatal but may be present in a mild form. Its chief interest at present lies in the fact that it explains pulmonary calcification, which was thought to be tuberculous but which gave a negative tuberculin test. The disease is caused by the *Histoplasma capsulatum* or an immunologically related organism. Skin tests with histoplasmin help make the diagnosis. With antigens derived from fungi, there is a possibility of crossed immunological response to coccidioidin and antigen derived from Haplosporangium.

Blastomycosis.—Blastomycosis may be caused by (1) Saccharomycetaceae and (2) Blastoporinae which are Hyphomycetes, the so-called Cryptococcus. *Cryptococcus capsulatus* of Darling is histoplasmosis. *Cryptococcus histolyticus* may involve the lung or may cause a cerebrospinal meningitis. A third variety pathogenic for man is *Cryptococcus hominis.*

If the disease is limited to a lobe or lobes or is present as a solitary tumor, lobectomy or pneumonectomy may be done. Iodides in increasing doses are given pre- and postoperatively.

Echinococcus Disease of the Lung (Hydatid Cyst).—Hydatid cysts are usually single. The cause is a small tapeworm, *Taenia echinococcus,* found in the intestinal canal of the dog, wolf, or jackal, which they ingested by eating organs of intermediate hosts—sheep and pigs. The ova are transmitted to human beings by handling infected dogs or ingesting uncooked, contaminated water or vegetables. A sac grows around an implanted embryo, forming a cyst. The embryo is usually implanted first in the liver. Here it forms a vesicle with an inner germinal layer and an outer laminated layer. From the germinal layer, vacuolated masses of cells (brood capsules) protrude into the vesicle's cavity. These in turn give rise to scolices. Daughter cysts are usually sterile and, without scolices or proliferaitng vesicles, are generally the result of mechanical infectious or toxic influence. If the cyst ruptures, it may be implanted in any organ in the body. Diagnosis is made by finding hooklets in the sputum. The x-ray findings are not characteristic. Aspiration is danger-

ous because of implanting cysts in the pleura and the so-called allergic reaction which may occur. There is usually an eosinophilia.

Treatment.—Formerly marsupialization was done and the cyst treated with 2 per cent formalin and packed with gauze. Now, after adequate preparation with penicillin and sulfadiazine, lobectomy is done.

Amebiasis.—Amebiasis may result in liver abscess (see Chapter 7). Pleuroperitoneal complications, though usually responsive to medical treatment (emetine and Diodoquin), may require surgical intervention. The indications for surgery are (1) bronchobiliary fistula; (2) empyema; (3) persistent amebic abscess of the lung; (4) collapsed lung. The surgical treatment is in general that of similar entities caused by other organisms plus the medical treatment of the disease. However, drainage is preferable to extirpation wherever possible even more so than in other conditions. This is because the organisms reside in the wall of the abscess and dissemination may result from radical surgery.

Neoplasms of the Lungs and Bronchi

Since many neoplasms of the lung originate in the bronchi, it is necessary that we consider lungs and bronchi together. Neoplasms of the lung may be benign or malignant, primary or secondary. They vary greatly in their structure because of the complexity of tissues, which embryologically make up its component parts. The following is a classification of the more common varieties:

I. Benign neoplasms (usually originate in the bronchi)
   1. Adenoma
   2. Papilloma
   3. Fibroma
   4. Lipoma
   5. Chondroma
   6. Osteoma
   7. Neurinoma
   8. Dermoid cysts
   9. Teratoma
   10. Cylindroma
   11. Hamartoma
   12. Hemangioma

II. Malignant neoplasms
   A. Primary
      1. Sarcoma
         (a) Spindle cell
         (b) Small round cell
         (c) Lymphosarcoma
         (d) Chondrosarcoma
         (e) Osteosarcoma
      2. Carcinoma nearly always bronchiogenic in origin; may be classified as to origin, distribution, and microscopic variety
         (a) Origin: [illegible] ic, from bronchial adenoma (adenocarcinoma, or oat cel[illegible]), from large bronchus, from small bronchi, from

blood vessels, from alveoli (alveolar cell carcinoma or pulmonary adenomatosis (see Chapter 15)

(b) Distribution: May be hilar (here in large bronchus, growth more or less restricted) diffuse infiltrative peripheral (here in small bronchus without cartilaginous walls grow fast and give rise to early metastases), miliary carcinosis, superior pulmonary sulcus of Pancoast (probably not a special type, but because of its location causes pain in shoulder girdle, Horner's syndrome, paralysis of hand muscles—Pancoast syndrome), alveolar cell carcinoma may be lobar or general.

(c) *Microscopic varieties:* May be *squamous cell, small cell (oat cell),* reserve cell carcinoma; adenocarcinoma; carcinoma simplex, hemangioendothelioma, alveolar cell.

B. Secondary neoplasms—may occur by *direct extension* from pleura or mediastinum or mediastinal nodes; metastasis more common way of transmission

(a) Lymphatic as from carcinoma of breast, lymphosarcoma, Hodgkin's, and lymphomas of leucemia

(b) Vascular as in sarcoma and carcinoma of thyroid, hypernephroma and chorioepithelioma; as part of a generalized carcinoma

Pathology of Benign Tumors.—The principal effect of benign tumors is that of obstruction which in turn may give rise to atelectasis, secondary infection (bronchitis, abscess, bronchiectasis). If the tumor is in the trachea and is sessile, it may give rise to stridor due to narrowing. If, however, it is on a pedicle, it may swing down, occluding the bronchus so that air cannot enter, but it can leave, giving rise to atelectasis, or it may swing up, allowing air to enter but it cannot leave, causing emphysema.

Lipomas arise from fat, which is a normal component of the major bronchi, that is present in the submucosal adipose tissue in the center of groups of bronchial glands and around them. Lipomas in the parenchyma of the lung or beneath the pleura arise from subpleural fat or fat in the smaller bronchi.

Adenomas arise from bronchial glands or their ducts in the larger bronchi. Graham suggests they be called "mixed tumors" because of the occasional presence of fat, cartilage, bone, or muscle (like the mixed tumors of the salivary glands). Often the adenoma resembles bronchiogenic carcinoma. Indeed it is a slow-growing, locally invasive neoplasm, which may at times metastasize or extend to regional nodes. Histologically mitotic figures and degenerative changes (pyknosis karyorrhexis) are not found in adenoma, but they are present in carcinoma. It is best to regard adenomas as slow-growing malignant neoplasms in most cases.

Cylindromas resemble the cylindromas of the salivary glands. Microscopically the tumor cells form tubules or cylinders filled with mucus. The main point of differentiation from bronchial adenoma, which cylindromas resemble very closely, is the presence of a mucoid secretion, apparently produced by the epithelial cells. They are as potentially malignant as the adenomas.

Fibromas are not common. As elsewhere, they are frequently associated with other cells, such as fat, muscle, and angiomatous tissue.

Chondromas and osteomas are rare and usually contain other elements.

Hamartomas are those tumors containing the normal components of an organ in an abnormal quantity, arrangement, and degree of differentiation. These are seen in the liver and other organs, including the lung. In the latter they are seen on microscopic examination to contain fat, bronchial mucosa, smooth muscle, and cartilage.

Symptoms and Signs.—Symptoms and signs are variable. Usually there is a cough which soon becomes productive and which may be accompanied by bleeding (adenomas). If atelectasis occurs, there is secondary infection, much sputum, and recurrent attacks of pneumonia. Often there is an asthmatic type of wheeze, particularly in sessile growths which do not move but partly obstruct the trachea or bronchus. Finally, bronchiectasis, pulmonary abscess, gangrene, or empyema may develop in neglected cases. The diagnosis is made by careful x-ray studies and bronchoscopic examination. Sometimes the growth will be shown by tomographic studies. More often an unexplained area of atelectasis leads to the supposition that the bronchial obstruction causing it is due to an endobronchial tumor, which is confirmed by bronchoscopy and bronchography.

Treatment.—Fibromas, chondromas, hamartomas, and lipomas should be removed by bronchoscope forceps, surgical diathermy, and implantation of radon seeds if necessary. If there are complications such as abscess or bronchiectasis, lobectomy may be necessary. Adenomas near the carina, those on narrow pedicles, freely movable adenomas, and those in poor-risk patients should be removed with the bronchoscope. If there is associated pulmonary disease, if the growth has recurred, if it is not accessible to the bronchoscope, or if there is seen to be adenomatous peribronchial infiltration, lobectomy or pneumonectomy is the safest treatment.

Pathology of Primary Carcinoma.—The pathology of primary carcinoma has been discussed in the classification of malignant neoplasms of the lung. The cause of pulmonary carcinomas is unknown. The miners of Schneeberg and Joachinetal are particularly susceptible. These mines contain radon, especially where pitch blend is mined. However, radon is not the sole cause. Contributing causes are pneumonoconiosis, chronic irritation, arsenic, radioactive substances, and, perhaps, hereditary susceptibility, since it is a father to son trade as well as much intermarriage.

Since practically all primary carcinomas originate in bronchial epithelium, it is proper to speak of bronchiogenic carcinoma. It is not rare and constitutes about 10 per cent of all carcinomas. The most frequent variety is the squamous-cell carcinoma. The next is the adenocarcinoma variety and the small-cell (oat-cell) type. The latter are thought to arise from bronchial adenoma. Since the growths start in the

bronchus, one of the first effects is bronchial obstruction which leads to atelectasis and secondary infection. Thus there are frequently such complications as pulmonary abscess, bronchiectasis, and pneumonia. These complications are often diagnosed while the carcinoma is missed. Biopsy sections do not always give a good guide to prognosis or operability. This is due to the fact that tissue sections vary from place to place. Ordinarily the squamous-cell type offers the best prospect of cure because its growth and metastasis are slower. Adenocarcinoma and the undifferentiated types are much more rapid in their progress and spread. Karsner believes that the hilic type, the diffuse infiltrative form,

FIG. 229.—Bronchiogenic carcinoma of the lung. Woman aged 48 years. Arrow points to a portion of the tumor mass which is projecting into the bronchus.

the peripheral form, and miliary carcinosis may represent, in part, different stages of the same process. Carcinomas that are grade 4 (Broders) are not so prone to spread by direct extension as are those of grade 3, but no predictions can be made on this basis alone. Alveolar cell carcinomas are extremely rare and the prognosis is poor although the tumor is slow growing.

Metastases of bronchial carcinoma are very frequent in the cerebrum. It is said that out of every nine tumors of the brain, one is metastatic and about one-third of these are from bronchiogenic car-

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cure patients of this disease, it should be suspected in any person who develops a chronic cough or wheeze with or without blood-streaked sputum if he does not have tuberculosis. *Aids in diagnosis* include: sputum examination, x-ray studies, bronchoscopy, bronchography, biopsy secured through the bronchoscope, or suspected supraclavicular lymph nodes, thoracentesis, and exploratory thoracotomy. Pneumothorax, punch biopsy, or thoracoscopy have been used as an aid to diagnosis. Sputum examinations should be done to rule out tuberculosis and to look for cancer cells which are found frequently if a careful search is made. X-ray examination and fluoroscopic studies are indispensable. The shadow of a central or a peripheral tumor mass, localized expiratory emphysema, localized atelectasis, mediastinal shift (usually toward the lesion due to atelectasis, rarely away, due to emphysema) are all indications of bronchiogenic carcinoma. Tomography: posteroanterior, lateral, and oblique views are necessary on some occasions. Bronchoscopy is done routinely in all suspected cases except (1) positive biopsy from a peripheral metastasis, (2) advanced state of the disease, (3) carcinoma cells in the sputum or pleural effusion, or (4) symptoms and signs sufficient to make the diagnosis, although with the latter instance corroborative evidence is usually obtained. Bronchography is usually not indicated, obscures the lesion, and may be the cause of extensive pneumonitis if the opaque oil is trapped beyond the growth.

Bronchoscopic washings often reveal cells stained by special technique (see Chapter 2); moreover the actual location of the growth may be more accurately ascertained by the site from which the washings were obtained.

The differentiation of primary and secondary carcinoma is sometimes difficult. The history of previous carcinoma elsewhere is by no means evidence that the lung lesion is secondary. If carcinoma is present in other organs, the logical conclusion is that of metastasis. More important are the "concealed" primary sites such as the kidney and adrenal which give little evidence of their presence until the lung lesion is found. In the rare case of metastasis to a bronchial wall, differential diagnosis may be very difficult. Peripheral, spherical lesions and multiple lesions are apt to be metastatic. In any event a careful examination should be made with gastrointestinal x-rays, pyelography, and gall bladder studies as indicated. Pulmonary resection may be indicated in solitary metastasis or even multiple metastases in one lobe. Therefore, if the *diagnosis is uncertain, exploratory thoracotomy* is in order.

The frequency with which carcinoma occurs in the presence of lung abscess, bronchiectasis, and tuberculosis makes one wary of accepting a final diagnosis on x-ray findings alone. However, the routine use of chest films as procured by state boards of health has been of inestimable value in detecting early lesions, thereby *allowing for early differential* diagnosis.

cinoma. Therefore, it is routine in some hospitals to make an x-ray study of the lungs in every case of brain tumor. Metastasis to the cerebellum is rare. Metastases may occur anywhere in the body but are usually seen in the regional nodes first. Other frequent sites are the pleura, mediastinum with recurrent nerve paralysis, cervical lymphatics with Horner's syndrome, phrenic nerve paralysis, vena cava obstruction, chest wall, esophagus, skin, peripheral nodes, liver, and lungs. Pleural effusion usually means pleural involvement and cancer cells are often found in this fluid.

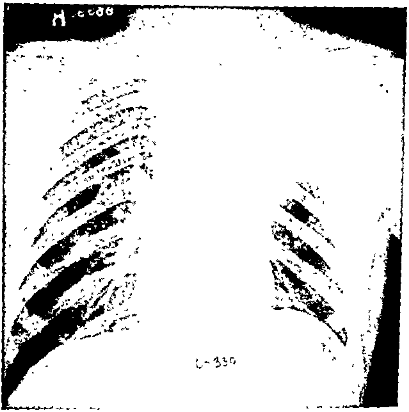

Fig. 230.—Carcinoma of the lung (primary). Superior sulcus tumor (Pancoast). Ultimately there are erosion of the ribs and a Horner's syndrome. The latter was present in this case. Note the elevation of the left leaf of the diaphragm. This may be due to phrenic narve involvement or to pulmonary atelactasis.

Symptoms and Signs.—Symptoms and signs are usually typical. There is a cough or wheeze or both with little sputum which is frequently blood streaked. There is often pain due to atelectasis. Later there are severe pains due to involvement of bronchial plexus, parietal or mediastinal pleura, bloody pleural fluid, loss of weight, paralysis of corresponding half of the diaphragm, paralysis of the left vocal cord (in the left-sided carcinoma) because of the proximity of the recurrent laryngeal as it passes around the arch of the aorta, brain symptoms due to metastases, and pulmonary osteoarthropathy. The late symptoms of carcinoma of the lung, like those of carcinoma of the breast, are of academic interest insofar as the probability of cure is concerned. Therefore, if we are to

(200,000) units of penicillin are left in the pleural cavity and the chest is closed in layers without drainage. The dead space is obliterated by organizing exudate and displacement of the mediastinum, diaphragm, and chest wall. Postoperatively the patients are placed in an oxygen tent for twenty-four to forty-eight hours. They are encouraged to sit up and cough by holding the chest.

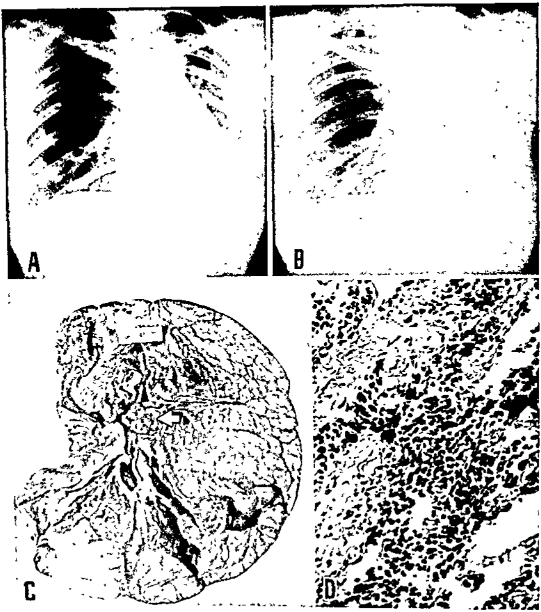

Fig 231 —Carcinoma of the left lung treated by pneumonectomy. R. F., a white woman aged 40 years, was admitted to the hospital complaining of a productive cough and dyspnea. *A.* X-ray photograph of the lung prior to operation. *C.* Photograph of gross specimen removed at operation. The arrow indicates the small cauliflower-like lesion *D.* Photomicrograph showing anaplastic carcinoma of the "oat-cell" variety. *B* Postoperative film. This patient has remained well to the present date which is now four years after surgery. (Case referred by Dr. R. R. Beach.)

Treatment.—Pneumonectomy in early cases. Every doubtful case should have an exploratory thoracotomy. Graham performed the first successful pneumonectomy in April, 1933. Unfortunately in our experience only about one-sixth of the cases are resectable when first seen. This rate will increase as diagnoses are made earlier. The mortality rate for the operation is about 10 per cent. The five-year "cures" are very few at present, averaging about 15 per cent or less as nearly as can be estimated. Lobectomy is rarely indicated but may be advisable for purely palliative reasons, or in doubtful cases of peripheral lesions with no nodal involvement.

Indications of inoperability are as follows: (1) Extensive pleural involvement evidenced by a bloody pleural effusion containing cancer cells. The fluid may be removed and replaced with air and then x-ray pictures taken to show pleural nodules; or punch biopsy with the thoracoscope may be done. We have preferred a small thoracotomy to the latter. (2) Extension to lymph nodes (supraclavicular, cervical and axillary). The nodes are easily removed for biopsy under local anesthesia. (3) Lymphatic dissemination as demonstrated by x-ray showing small nodules beneath the visceral pleura or by thoracotomy. (4) Hematogenous spread to liver, bones, and brain as determined by physical signs or x-ray. (5) Pain down the arm, Horner's syndrome (see Chapter 18), and erosion of first and second ribs which is known as Pancoast's syndrome or superior sulcus syndrome. (6) Nerve paralyses such as the recurrent laryngeal and phrenic which may be operable but usually not curable. (7) Small-cell types which should be given the benefit of surgery although the prognosis is poor. (8) Extension to the chest wall renders the lesion hopeless so far as cure is concerned, but palliation may be obtained by resection of the intercostal nerves or chordotomy or resection of the involved chest wall along with pneumonectomy.

The patient is prepared for operation by using penicillin by inhalation and intramuscularly. Sulfadiazine is given by mouth. Blood transfusions are given or indicated and blood is given by ankle vein during surgery. Intratracheal anesthesia is used but first the trachea and bronchi are aspirated and then kept clean throughout the operation. Ether and oxygen are used and at the conclusion of the operation the trachea and bronchi are again aspirated. A posterolateral incision is made and the fifth and sometimes the sixth ribs are resected. The patient's head is lowered to promote drainage. After freeing the lung, when adhesions are present the hilus is dissected out, the pulmonary artery and veins are individually ligated with No. 2 silk, and then the main stem bronchus is divided close to the carina and the lymph nodes and the lung are then removed. The bronchus is closed with interrupted silk sutures, approximating the membranous to the cartilaginous portion. Bronchial vessels are tied with silk. If possible, the mediastinal pleura is used to cover the bronchial stump. Two hundred thousand

the pharynx. The probe is pushed through and the fistula everted into the pharynx and then tied off.

True branchial cleft fistulas are lower than the hyoid bone and are lined with skin, hair follicles, and sebaceous and sweat glands. They should be excised.

Thyroglssal duct cyst will be discussed in Chapter 22 in conjunction with aberrant thyroids.

Submaxillary and submental inclusion cysts form from the small budlike lobules which go to form the gland. Should these tubules become obliterated, cysts will occur which should be removed with the gland, if necessary.

Infections of the Neck.—Infections of the neck are discussed in the paragraphs on mediastinitis which follow this chapter.

New Growths of the Neck.—New growths of the neck are many and varied. The persistent branchial cleft or thymic duct may rarely become the seat of squamous carcinoma. The lymph nodes are often a part of the lymphoblastic group of diseases discussed in Chapter 17.

Adamantinomas belong to the oral cavity and are reviewed in Chapter 19. Salivary gland and thyroid neoplasms are important and will be described in Chapter 22. Sarcomas and carcinomas of the mandible, metastatic growths in the lymph nodes, and secondary involvement of the neck from a malignant growth in the pharynx must be kept in mind in all tumors in the neck.

The Larynx

The voice box is a cartilaginous chamber in the neck, often referred to as the "Adam's apple." At its entrance are the two vocal cords, between which is an opening (the glottis), through which we breathe. The entrance of food into the larynx is prevented by the contraction of the thyrohyoid muscle which raises the organ, bringing the glottis under the shelter of the epiglottis and the base of the tongue. The latter is not essential since after its removal food still does not enter the larynx. The epiglottis stands erect and food passes over its posterior (not anterior) surface. The elevation of the larynx is important and if fixed by disease, food finds its way into the larynx. At the same time that the larynx is pulled up, the vocal cords are approximated due to the contraction of the arytenoid cartilages which are thereby drawn forward against the posterior pharyngeal wall and rotated medially. This has the effect of closing the glottis and opening the upper end of the esophagus. When the constrictors contract on a bolus of food, it follows the path of less resistance and goes down the esophagus.

The chief nerves supplying the larynx are the superior and inferior laryngeal (recurrent) nerves. The latter is unusual in that it is composed of two sets of fibers carrying impulses which produce opposing muscles action—abduction and adduction and also coordinated impulses concerned with speech and breathing. Paralysis of both recurrent nerves results in inability to abduct or adduct the vocal cords. When the recurrent laryngeal nerves are injured, the cords are lax and cannot be abducted or adducted. There is no difficulty in breathing, but there is inability to speak. Within three to six months the voice returns due to atrophy and the resultant fibrosis which tends to pull the cords together as the scar contracts. This continues until the cords are brought almost into approximation. Then there is difficulty in breathing on the slightest exertion and actual air hunger, if large amounts of air are necessary. This is often

X-ray treatment of pulmonary carcinoma is used as a palliative measure but is not curative. Secondary carcinoma is not treated by resection, although when the primary lesion can be removed, as in carcinoma of the stomach, and when there is one or more metastatic nodules, in one lobe, lobectomy has been done. This may prolong life.

THE UPPER RESPIRATORY TRACT

Embryology

About the second week of fetal life, *the foregut develops five pouches from the* interior lateral walls. These are known as the branchial pouches. At the same time the ectoderm becomes indented over the corresponding pharyngeal pouches. These are known *as the branchial* grooves. The pouches and grooves *come together so* that ectoderm and entoderm are in contact, the contracting area being the closing membrane which disappears in animals with gills, forming gill clefts, which open from the pharynx *to the exterior*. The mesoderm is thus pushed aside into six cylinders, *the* branchial arches, of which the first two partially telescope over the remainder, forming the cervical sinus. Each arch contains a cartilaginous bar and in each is the forerunner of the primitive aortic arches. (See Chapter 17.) The following is a list of the arches and their ultimate structures: *First*, or mandibular, arch—muscles of mastication, lower lip, mandible, anterior part of tongue; from the cartilaginous portion comes part of middle ear and mandible; *second*, or hyoid, arch—structures of upper part of the neck and *from* its cartilage the styloid process, styloid ligament, lesser cornu of the hyoid bone, and, with the third arch, the body of the hyoid and posterior part of the tongue; *third*, *fourth*, and *fifth* arches—structures in the vicinity of the *hyoid*, whereas, the *sixth arch* gives *origin* to the *cricoid*, arytenoid, and tracheal cartilages.

All the branchial grooves disappear except the first, which gives origin to portions of the auricle and external acoustic meatus.

The *four pairs of pharyngeal pouches are important* for they form, respectively, the following adult structures: (1) the auditory (eustachian) tubes and tympanic cavity and tympanic membrane, (2) the palatine tonsils, (3) the thymus anlages, (4) the parathyroids and epithelial bodies (*see Chapter 22.*)

The Neck

Congenital Anomalies of the Neck.—From the third pouch, two tubes descend into the mediastinum to form the thymus. They course downward and medially along in the anterior *border of the sterno-mastoid, lateral to the thyroid, and anterior to* the carotid sheath. Sometimes these tubes persist as a sinus, a cyst, or a fistula, depending on whether their distal end is open, ending a short way up, or both ends are closed or both ends are open, the internal end opening in the tonsillar fossa. This branchial cyst or fistula is probably the thymic ducts. The tract is lined with ciliated and squamous epithelium and surrounded by connective tissue. Mucoid or milky material or pus exudes from the branchial sinus or fistula. If there has been a tonsillectomy, liquids ingested may in part drool from the fistula. The treatment is complete excision. The tract may be injected with methylene blue but *this is* rarely necessary. A probe is *introduced and the dissection* carried up to

opposite side. Inferiorly it passes down on the surface of the bodies of the vertebra into the posterior mediastinum. From the sheath of the vessels outward beyond the posterior edge of the sternomastoid muscle the prevertebral fascia covers the scalene muscles, the brachial plexus, and the subclavian artery. On reaching the clavicle, the fascia is attached to its upper surface where it blends with the superficial layer, and then it is continued down over the subclavian muscle, forming its sheath, and ends in the costocoracoid membrane. The part over the subclavian artery and vein is continued over them and the brachial plexus and follows them into the axilla. This layer of fascia forms the floor of the posterior cervical triangle, and the roof of this triangle is formed by the superficial layer of the deep cervical fascia. Between these two layers the subscapular artery and veins run. The descending branches of the cervical plexus, the spinal accessory nerve, the omohyoid muscle, some fat, and lymph nodes are found here.

The pretracheal layer passes from side to side in front of the trachea. Laterally it, too, blends with the sheath of the vessels and is continued posteriorly behind the pharynx and esophagus as the buccopharyngeal fascia. In front it blends in the median line with the superficial fascia and is attached to the hyoid bone and cricoid cartilage. It splits to enclose and form a capsule for the thyroid gland and the inferior thyroid veins, and thense it passes to the arch of the aorta to be continuous with the pericardium. Laterally, it passes under the sternohyoid, omohyoid, and sternothyroid muscles to blend with the sheath of the vessels.

The buccopharyngeal fascia which was mentioned above lies between the pharynx in front and the vertebral column behind. This is known as the retropharyngeal space. The fascia forming the posterior wall of this space is the prevertebral fascia. Forming its anterior wall is a thin layer of connective tissue called the buccopharyngeal fascia. It invests the superior constrictor of the pharynx and is continued downward on the buccinator muscle. It is continued downward behind the pharynx and esophagus into the posterior mediastinum. Laterally, it blends with the sheath of the vessels and is continuous with the pretracheal fascia around the larynx, trachea, and thyroid gland.

Collections of fluid and pus superficial to the deep fascia tend to perforate the skin and to be discharged externally. Exudates in the supersternal notch or the space of Burns bulge anteriorly but may perforate posteriorly. The sternothyroid and sternohyoid muscles are attached to the posterior surface of the sternum, but the layer of fascia on their anterior surface is very thin so that pus may pass between the muscles or perforate them and go down in front of the pretracheal fascia close to the undersurface of the sternum. It would then tend to show itself in the upper intercostal spaces close to the sternum. Exudates between the pretracheal and superficial layers as may occur from an abscess of the thyroid gland tend to work their way downward. The pretracheal fascia at the sides blends with the sheath of the vessels and the fascia covering the posterior surface of the sternomastoid muscle. Pus can follow the posterior surface of the muscles behind the sternum in front of the innominate veins and arch of the aorta. Transudates and exudates between the pretracheal and prevertebral layers cannot go further to one side than the sheath of the vessels; therefore, they follow the trachea and esophagus down into the posterior mediastinum. This space between these layers is sometimes called the visceral space because it contains the esophagus, trachea, and thyroid gland. Pus in this space may also perforate into the trachea, pharynx, or esophagus, or even externally and involve the great vessels. If the anterior portion of the thyroid gland suppurates, the pus may perporate the thin pretracheal fascia covering it and pass down behind the sternohyoid and sternothyroid muscles into the anterior part of the superior mediastinum.

Exudates posterior to the prevertebral fascia, as from caries of the vertebrae if high up, bulge into the pharynx, forming a retropharyngeal abscess. Such exudates may follow the scalinae muscles and brachial plexus down around the axillary artery into the axilla. In the neck they show themselves posterior to the carotid arteries and to the outer edge of the sternomastoid muscle. Exudates in the sheath of the great vessels, when originating from lymph nodes may, first raise the sternomastoid muscle and show along its anterior border. They may perforate the vessels or pass down along the vessels into the superior mediastinum or may bulge into the visceral space between the prevertebral and the pretracheal layers and follow the trachea and esophagus down into the chest. Should they tend outwardly, they may break into the posterior cervical triangle between the prevertebral and superficial layers and show above the clavicle.

Retropharyngeal abscess comes from diseases of the vertebrae or from lymph nodes which are suppurating or from contiguous spaces as outlined in the text. An abscess here may point into the pharynx or, pushing its way outward, pass behind the great vessels and show itself behind the outer edge of the sternomastoid muscle. When originating in the retropharyngeal space it lies in front of the prevertebral fascia and behind the buccopharyngeal fascia. It either points into the pharynx or going down follows the posterior surface of the esophagus into the posterior mediastinum. It may also perforate the esophagus. Pus in the posterior cervical triangle, if above the prevertebral layer, bulges directly forward and tends to open through the skin. Its progress downward is obstructed by the attachment of the superficial layer to the top of the clavicle as it blends with the prevertebral layer. If pus is beneath the prevertebral layer, it may then follow the brachial plexus and subclavian artery down beneath the clavicle and appear in the axilla. The attachments of the costocoracoid membrane tend to direct the pus laterally under the pectoralis minor muscle into the axilla rather than to allow it to come forward on the anterior portion of the chest.

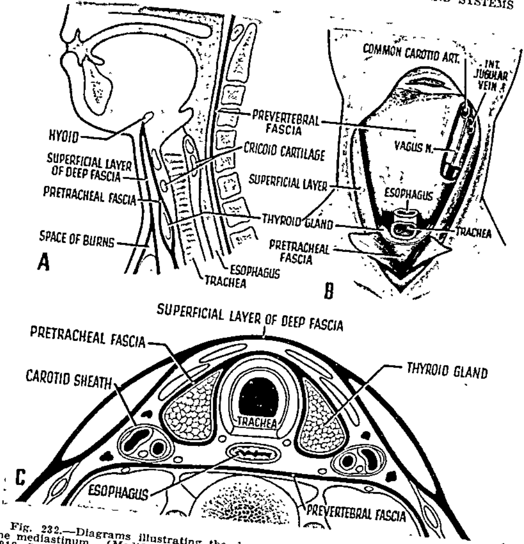

Fig. 232.—Diagrams illustrating the deep cervical fascia and its prolongations into the mediastinum. (Modified from Davis, G. B.: Applied Anatomy, ed. 5, Philadelphia, 1918, J. B. Lippincott Co., and Cunningham: Manual of Practical Anatomy [revised by Robinson, A.], ed. 6, New York, 1914, William Wood & Co.)

A, Sagittal section illustrating continuity of deep cervical fascia and pharyngeal spaces.

B, Longitudinal section showing the superficial layer, the pretracheal layer, and the prevertebral layer of the deep cervical fascia as it is prolonged down into the mediastinum.

C, Transverse section of the neck through the sixth cervical vertebra showing the compartments.

The cervical fascia may be divided into three layers: the superficial, which completely encircles and envelops the neck, the prevertebral, which passes from side to side in front of the spinal column, and the pretracheal layer, which passes from side to side in front of the trachea.

The superficial layer is attached above to the occipital bone and the mastoid process, and it blends with the capsule of the parotid gland, then passes to the angle of the jaw and along the body of the mandible to the symphysis, where it proceeds in the same manner to the opposite side. Below, it is attached to the sternum, the under edge of the clavicle, the acromion process, the spine of the scapula, and then across the vertebral spines and to the ligamentum nuchae and is attached to the external occipital protuberance. In the front of the neck it passes from the mandible down to be attached to the hyoid bone and then down to the sternum and clavicle. About 3 cm. above the sternum the fascia splits into two layers, one to be attached to the anterior and the other to the posterior edge of the sternum in front of the sternohyoid and sternothyroid muscles. Between these two layers is the space of Burns. It contains the lower ends of the anterior jugular veins with the branch that joins them, some fatty tissue and lymph nodes, and the sternal origin of the sternomastoid muscles.

The prevertebral layer passes from side to side in front of the bodies of the vertebrae. It covers the muscles attached to the spine. On reaching the carotid artery and jugular vein, it helps to form their sheaths. Its upper edge is attached to the base of the skull at the jugular foramen and carotid canal and thence across the basilar process to the

(Continued on opposite page)

nels. The causes of obstruction within the lumen of the bronchi may be listed as endogenous or exogenous. The former may be due to (1) tenacious sputum, (2) fibrinous casts, (3) broncholiths, (4) ruptured lymph nodes, (5) postoperative retention of secretions, (6) the entrance of a foreign body of any type occluding the lumen of the bronchus, the most important exogenous cause.

Obstruction due to changes in the bronchial wall may be listed as follows: (1) congenital anomalies of the bronchi; (2) inflammatory diseases of the bronchi which may be nonspecific or specific; the former are inflammations of the bronchial mucosa or cicatrization following chemical burns or ulcers—the latter may be due to tuberculosis, syphilis, leprosy, and rhinoscleroma; (3) new growths which may be benign or malignant; (4) distortion of bronchi by kinking or twisting as the result of a pulmonary disease, vertebral disease, or intrathoracic dislocation of the viscera following pneumothorax, thoracoplasty, pneumonectomy, or lobectomy.

The extrabronchial causes for obstruction are (1) enlarged lymph nodes of inflammatory or neoplastic origin, (2) mediastinal suppuration, mediastinal emphysema, mediastinal neoplasms or cysts, (3) vertebral disease which may be inflammatory or neoplastic, (4) neoplasms of the lungs, esophagus, or intrathoracic goiters which may produce an obstruction, (5) cardiovascular disorders such as aneurysms of the aorta or the pulmonary arteries; also congenital anomalies of the cardiovascular system producing pressure upon the trachea. (Chapter 17.)

The results of bronchial obstruction are variable. If the obstruction is complete, no air will get into the lung, which is supplied by the bronchi, and atelectasis will result. If it is incomplete, there may be great dilatation beyond the point of obstruction and there may be great hypertrophy of the muscular elements, or if a ball valve type or flap door type of obstruction is present, cavitation may result. Such cavities will not collapse spontaneously by external pressure or drainage. Furthermore, after obstruction to the bronchus, the portion distal to the occlusion not only dilates but also retains secretion which becomes a favorable medium for the growth of bacteria, so that it is not uncommon to see such complications as pneumonitis, lung abscess, bronchiectasis, or bronchiectatic cavitation. This is also true in tuberculosis, as we have seen in Chapter 8. See Chapter 15—Cohnheim's laws.)

Bronchial obstruction may be compared in a general way with obstructions elsewhere in the human body. When the obstruction is sudden and complete, there is usually atelectasis distal to the obstruction, and this may be permanent and may produce changes, as we have seen, due to the atelectasis. When it is incomplete, there may be dilatation distal with retention of secretions and a great amount of fibrosis and hypertrophy of muscular elements. When it is of an incomplete and ball valve nature, there will be great dilatation and formation of all types of cavities.

accompanied by a crowing or roaring sound. The treatment is nerve suture if discovered early. Later the arytenoid muscles may be shortened on one side, making the glottis larger.

Diseases and Injuries of the Larynx.—*Foreign bodies* are frequently aspirated into the larynx. This is dangerous because asphyxia may occur. Removal of these bodies is often carried out through the use of the *laryngoscope.* Sometimes their removal may be accomplished with the fingers or a hemostat or by turning a child "upside down" to facilitate extrusion by cough. Should all methods fail, or should the larynx be obstructed by new growth or stricture, a tracheotomy must be done. *Intubation* was formerly used in laryngeal diphtheria or edema for temporary help. It is safer and less irritating to do a tracheotomy. Inflammations may be simple (laryngitis) or specific (tuberculosis, syphilis). *Laryngitis* is treated by steam inhalations, such as compound tincture of benzoin; specific infections are treated by specific treatment (syphilis) or general treatment (tuberculosis). Recently a few cases of laryngeal fibrosis and scarring have been reported from the use of the duodenal tube. This is due to irritation of the cricoid with resultant perichondritis. It may be avoided by using small, soft tubes, which should be removed at frequent intervals and then reinserted if necessary.

New Growths may be benign (papilloma) or malignant (carcinoma). These may be removed locally, or, if extensive, the entire larynx must be extirpated (*laryngectomy*) after a permanent tracheotomy has been established. Electric speaking devices are available for such patients.

The Trachea and Bronchi

The trachea and bronchi are the tubes through which we breathe. The trachea can be easily felt in the neck just above the manubrium sterni and below the cricoid cartilage. It is surrounded by cartilaginous rings except posteriorly, where it lies on the esophagus. The mucus membrane is made of columnar epithelium bearing small hairlike cilia, which help trap foreign bodies, such as dust, until they may be coughed up. The trachea begins in the larynx and divides into the right and left main bronchi at about the level of the fifth thoracic vertebra. These bronchi are smaller than the trachea but much like it in structure. The right is in more direct line than the left. The bronchi lose their cartilaginous nature as they divide and subdivide into bronchioles.

Bronchial Obstruction

Bronchial obstruction is important not only because of the intrinsic factor which is causing the obstruction, but more because of its effects on the bronchi and lungs. As in all hollow tubes, the obstruction may be within the lumen of the tube or it may be outside the tube, producing pressure. We have used this same general classification in obstructions of the bowel, blood vessels, common bile duct, ureters, and other chan-

nels. The causes of obstruction within the lumen of the bronchi may be listed as endogenous or exogenous. The former may be due to (1) tenacious sputum, (2) fibrinous casts, (3) broncholiths, (4) ruptured lymph nodes, (5) postoperative retention of secretions, (6) the entrance of a foreign body of any type occluding the lumen of the bronchus, the most important exogenous cause.

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Foreign Bodies.—Foreign bodies are aspirated into the trachea and bronchi frequently. This is especially true in children. All sorts of objects have been recovered. Dr. Chevalier Jackson has catalogued these into food, hardware, jewelry, etc. Due to his efforts, bronchoscopy has

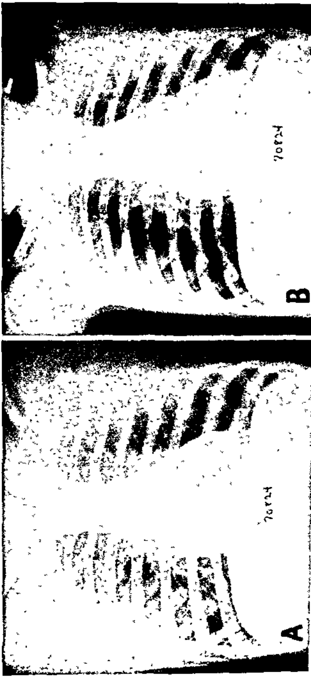


Fig. 233.—*A*. Nonopaque foreign body of the right mainstem bronchus. X-ray taken during *inspiration*. *B*, Same case. X-ray taken during expiration. There is an obstructive emphysema on the right, with partial collapse on the left. The right diaphragm is not elevated to the normal position. The heart is pushed over to the left, as is also the trachea.

been developed. The diagnosis is made from a history of aspiration of an object and a cough. In children any persistent cough must be investigated carefully by x-ray examination, which will easily reveal some foreign bodies, and, if the x-ray is negative, by bronchoscopic examination. A foreign body may cause a pulmonary abscess or erosions into a

large vessel; or rarely the object may be encapsulated or extruded into a bronchus or the pleural cavity.

Broncholiths.—Broncholiths (bronchial stones, bronchial calculi) are hard gritty fragments of calcium phosphate or calcium carbonate which are occasionally coughed up by patients who have bronchiectasis, lung abscess, anthrasilicosis, or other chronic inflammatory diseases. The source may be from (a) the lungs, (b) the bronchi, (c) the peribronchial lymph nodes. Calcifications occur in caseous tuberculous areas in the lungs or lymph nodes, old abscess cavities in the lung, chronic empyema, and histoplasmosis areas. Calcified areas erode through the bronchus and ultimately behave as a foreign body. While in the process of erosion, there may be persistent cough with some hemoptysis and much sputum.

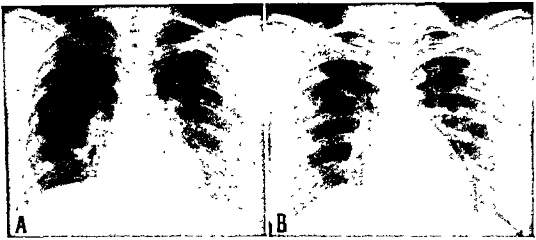


Fig. 234.—Broncholithiasis. Miss R. H., aged 26 years, complained of chronic productive cough with repeated hemoptysis. Patient had coughed up small broncholith on one occasion. Massive hemorrhage brought her to the hospital. After bleeding had ceased, bronchoscopy was done and a part of the broncholith was removed from the right middle lobe bronchus. Symptoms continued and atelectasis of the right middle lobe ensued. Thoracotomy and right middle lobectomy was done. The broncholith had eroded through the medial branch of the middle lobe bronchus and had engendered much fibrosis, occluding the lateral branch at its junction. The patient made a smooth recovery. Pathology report: Broncholithiasis, middle lobe showing complete ateleectasis, carnification with fibrosis, chronic pneumonitis. The term carnification is from *caro, carnis,* flesh, and *facere,* to make. Carnification is due to consolidation, and the term is used to describe the meaty appearance of the lung resembling muscle. *A.* Arrow points to broncholith. No atelectasis at this time. There are also calcified areas in the upper and lower lobes. *B.* Postoperative x-ray after middle lobectomy. (Case referred by Dr. R. Henry.)

Treatment.—The treatment consists of removal of the object by the use of the bronchoscope with long, specially designed forceps. Even lung tissue may be penetrated, and it is not unusual for the bronchoscopist to remove a pin from the main stem bronchus. Occasionally the surgeon will be guided by the bronchoscopist and will enter the lung through an intercostal incision to remove an extrabronchial foreign body. Complications such as lung abscess and bronchiectasis are treated as outlined elsewhere in this chapter.

Bronchiectasis

Bronchiectasis is a disease of the bronchi (in one or more lobes or segments) characterized by dilatation and infection. We have all been the victims of an acute bronchitis, with its fever, malaise, and persistent cough. Finally we are able to cough up the mucus and we feel better. In bronchiectasis this coughing-up process continues. The cause is unknown. However, the following is a list of possible contributory causes: sinusitis and disease of the accessory air passages, infections of the bronchi and lungs (recurrent bronchitis, acute and chronic, measles, whooping cough, scarlet fever, influenza, pneumonia, lung abscess, pleurisy, tuberculosis) cystic disease of the lungs, bronchial obstruction from any cause (foreign body, broncholithiasis, carcinoma or benign tumor of bronchi, etc.), the effects of bronchial obstruction (atelectasis or emphysema with infection), situs inversus with sinusitis "Kartegener's syndrome") has been a rare combination preceding bronchiectasis. In over 25 per cent no contributory cause is discovered. The pathological factors are also varied. Some observers say it is due to a chronic infection, with obstructing mucous plugs, persistent cough, and a subsequent dilatation or an obliterative bronchiolitis with fibrosis. Others believe the bronchi are pulled and held open by peribronchial fibrosis. Still others claim that it is due to a congenital weakness of the bronchial wall. The bronchi becomes destroyed and are replaced largely with fibrous tissue. This destructive process extends into the surrounding lung and the end result is a set of rigid tubes in a rigid cavity.

Behind the various causes and changes is the following over-all picture: The bronchi are dilated due to pulsion or traction, the former more than the latter. In pulsion types, bronchial obstruction is the usual cause. Cough alone does not do it, but cough with mucous or other plugs is probably at fault. If this is true we may infer that most bronchiectasis begins in childhood, and if this is true, more attention should be paid to whooping cough, measles, and bronchitis with the thought that postural drainage and breathing exercises may prevent the disease to some extent. Traction bronchiectasis is seen in chronic lung abscess, chronic empyema, and cavitary tuberculosis; almost invariably in lobectomy for chronic lung abscess there is extensive lung fibrosis and bronchiectasis. Here the bronchi are actually "held open" by fibrous tissue contraction. It is probably fair to say that in all cases both processes are at work. Even in the so-called congenital types this may be true because respiration does take place to a limited extent in utero, and also cystic disease due to congenital malformation may be present.

Gross changes are easily seen. The bronchi are dilated into various shapes and types: cylindrical, fusiform, saccular, and cavitary. There is thickening of the bronchial wall with vascular papillary projections of the mucosa. This may be due to proliferation or to uneven destruction as is present in chronic ulcerative colitis, for example. The lung parenchyma

is replaced to a great extent by fibrous tissue. Blood and pus are seen to exude from the infected bronchi. The process may involve any lobe of the lungs but is usually in the lower lobes and more in the basal than the apical segment. Abscess of the lung is more common in the apical segments. The left lower lobe and lingula account for about one-fourth of our cases. Both lower lobes may be involved and sometimes the disease involves both lungs.

Microscopic alterations include hyperemia, fibrous proliferation of fibrous tissue, destruction, and much granulation tissue. Glands, muscle, elastic tissue, and even cartilage may be largely destroyed and replaced by fibrous tissue. Thus normal bronchial contractility is lost, and under

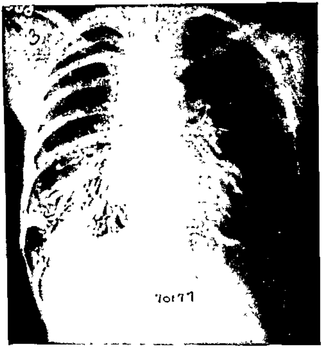


Fig 235.—Bronchiectasis. Lipiodol injection, showing dilatation, obstruction, and sacculation of the bronchi.

the influence of collecting secretions and cough, further dilation is inevitable, such as a hernia resulting after infections in an abdominal wound, which has healed by second intention. The epithelial lining is partially destroyed and perforations are seen. Blood vessels may rupture, giving rise to hemoptysis, or become thrombosed, causing embolism and brain abscess. Areas of atelectasis and compensatory emphysema may be observed about the primary zone. The disease remains static so far as the lobe or segment involved is concerned but is progressive within the segment. Bacteria of all types are found, including cocci, spirochetae, and fusiform bacilli.

Symptoms and Signs.—The principal symptom is a persistent productive cough with thick purulent malodorous sputum. Patients soon

learn that their breath is foul, not only to themselves but to others, and therefore the "inhibited personality type of patient in bronchiectasis" has been described. If the disease develops in early childhood, adult age is not ordinarily reached without treatment. It is true that there are all

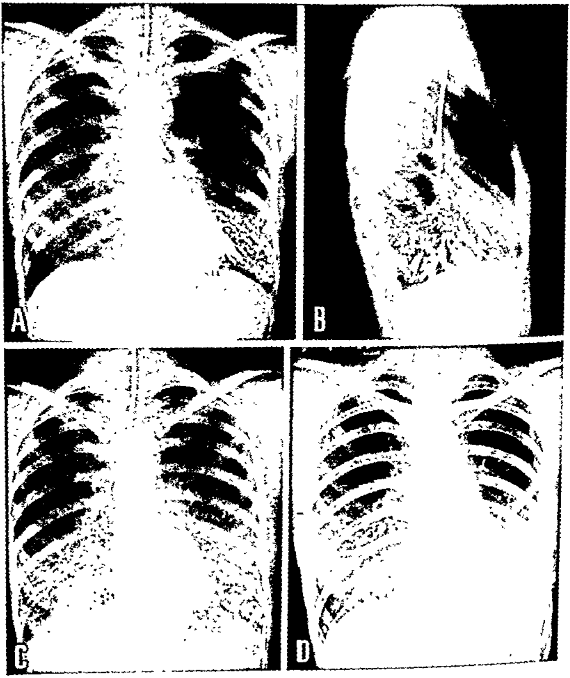


Fig. 236.—Bronchiectasis. Preoperative and postoperative x-ray pictures of F. G., a woman aged 26 years, with left lower lobe bronchiectasis and bronchiectasis of the lingula. The patient had a chronic, persistent cough with productive sputum which at times amounted to 10 ounces per day. *A*. Preoperative posteroanterior film showing extensive bronchiectasis of the left lower lobe and lingula following the introduction of Lipiodol by catheter (bronchogram). *B*. Lateral view. *C*. Bronchogram of right lower lobe. At operation a lower lobectomy and lingulectomy were performed by the individual hilar ligation technique. *D*. Postoperative film seven days after surgery. (Case referred by Dr. R. Henry.)

gradations in symptoms, from a productive cough only in the presence of an upper respiratory infection to coughing spells especially in the morning, of two to three hours, accompanied by hemoptysis, vomiting, and collapse. The slightest exertion produces dyspnea in advanced cases.

Physical signs are so varied that they may resemble any lung condition—usually there are dullness and moist râles and diminished breath sounds which may vary in intensity over different areas and vary from day to day. Later there is emaciation, anemia, general weakness, clubbing of the fingers (pulmonary osteoarthropathy). Bronchospirometric determinations reveal the pulmonary reserve in the good lung or in the better of the two and the extent of functional tissue in the affected side.

X-ray examination and fluoroscopic studies are essential to proper diagnosis. There will be areas of atelectasis, emphysema, dilated bronchi. The fluoroscope permits inspection in the posteroanterior, lateral, oblique, lateral decubitus, and Trendelenburg positions, so that every portion of the lung, including the posteromedial costovertebral area and medial diaphragmatic zones, will be seen and atelectasis found if present.

Bronchography is useful to determine the extent of the bronchiectasis and in some cases, especially postoperative (lobectomy cases, pneumonotomy) and congenital cystic disease, it may be necessary in the differential diagnosis of lung abscess, localized empyema with bronchopleural fistual, and congenital cystic disease of the lung and saccular bronchiectasis.

It is well to remember that Lipiodol is not innocuous and that after its use the oil may remain as a source of irritation if emphysema is present. Also after it passes a partially obstructed bronchus, it will not be coughed up from tension cavities, large abscess cavities, or saccular bronchi and must be removed with the lesion. It is conceivable that more lung tissue than is involved by the disease will have to be removed after its use.

Bronchoscopic examination is done routinely because it shows the main sources of exudate, areas of acute inflammation, tumors, or foreign bodies. Prior to operation the patient coughs up all of the sputum he can and then bronchoscopic aspiration is done to remove as much secretion and exudate as possible. Some surgeons prefer to operate in the afternoon because the patient will have emptied the bronchial tree of exudate by this time.

Treatment.—Treatment consists in general care—nutritious foods, fresh air, sunshine, and ample rest—and postural drainage, which must be prolonged. Above all, there must be tireless perseverance. In children a special iron frame covered with canvas is used. This is tilted at intervals, permitting easy expectoration. Bronchoscopic aspiration helps. Penicillin and streptomycin intramuscularly and by inhalation is of great value in early cases. If the bronchiectasis is symptomless (diagnosis by bronchography), medical management alone will give good results. In extensive cases, where all lobes are involved, or in those patients, usually

over 50 years, in whom the cardiorespiratory reserve is too poor to attempt surgery, medical treatment is indicated. In all others surgery should be done.

Surgical Treatment.—Preoperative preparation of a patient for lobectomy is designed to put the lungs in the most favorable condition possible and to improve general health. To accomplish the former, the lungs must be kept empty of their exudates by postural drainage and bronchoscopic aspiration if necessary, sinuses are treated if infected, pleural infections are drained, and bacterial flora are reduced by inhalation of penicillin, which is also given intramuscularly with streptomycin for three to four days. The general health of the patient is improved by attention to the focus, but, in addition, the anemia, which is usually present, must be combated by a nutritious diet and blood transfusion. Vitamins B and C are given and attention is paid to water and protein balance. Sulfadiazine is given by mouth in large doses (3 to 4 Gm. daily) to control bacteremia.

FIG. 237.—Pneumonectomy for extensive bronchiectasis and chronic empyema. K. K., a 7-year-old girl, had left lower bronchiectasis with productive cough since the age of 4. *A left lower lobectomy was done elsewhere, but the child continued to cough.* She had episodes of chills and fever and had lost much weight. Bronchoscopic and x-ray studies showed extensive saccular bronchiectasis of the remaining upper lobe. Upper lobe removed and parietal decortication done over the old empyema cavity. Portions of the fourth, fifth, and sixth ribs were removed and muscle flaps used to close the cavity. X-ray shows condition about one year after surgery. The child is well and has gained much weight. She is attending school and plays with other children without restriction. Note the position of the trachea and the stump of the left main stem bronchus. (Case referred by Dr. R. Henry and Dr. H. Call.)

The *operation* is conducted under ether-oxygen endotracheal anesthesia, or nitrous oxide-oxygen anesthesia supplemented with curare. Patients are placed in 20 to 30 degree Trendelenburg position with the operative site upward. *This favors drainage of mucopus into the*

pharynx where it may be aspirated by the anesthetist. A reverse position is used in bilateral bronchiectasis so that the secretions from the lung tissue being removed will gravitate to the dependent infected lobe of the other side instead of into the trachea, causing suffocation. We have been impressed with the prone position on the table with special upper chest and pelvis rests. This allows free breathing and all secretions find easy exit.

Posterolateral or anterolateral incisions are made, depending on the choice of the surgeon and the lobes involved. For lower lobes, the seventh rib is resected and subperiosteally and for upper lobes, the fifth. Incisions are made through the bed of the rib. Intercostal incisions may be used in thin persons or children but in our hands have given insufficient

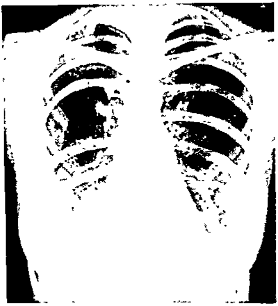


Fig. 238.—Although bronchiectasis is sometimes limited to pulmonary segments, permitting segmental resection of the lobe, very often it involves not only segments but lobes as well. Moreover, it may be bilateral, requiring bilateral resection. The above film illustrates the case of B. M., a girl 20 years of age, who has been an invalid since the age of 12. There was a persistent productive cough with great and extensive clubbing of the fingers, extreme weight loss, and chronic and persistent fever. She had been in and out of hospitals many times. Medical treatment, postural drainage, and all varieties of conservative management had been tried prior to the advent of pulmonary resections. These were unavailing. The patient was operated upon in two stages; the right lower lobe and middle lobe were removed first and then approximately six months later the left lower lobe and lingula were removed. The x-ray picture shows the present condition. This patient who had been incapacitated most of her life is now married and the mother of a child In addition, she is able to take care of her home and family. (Case referred by Dr. L. Levi.)

exposure in many cases. Segmental resections may be used in some cases but usually this will be restricted to the lingula. As our knowledge concerning pulmonary segments improves, more and more lung tissue may be spared. The individual ligation technique is used wherever feasible as is true in surgery of other organs.

During the operation, blood and fluids are given as required through an ankle vein. If necessary, an arm vein may also be cannulized so that

if a large amount of blood be needed, it may be given quickly. Before closing the chest, the lung is re-expanded and penicillin 500,000 units, is left in the chest cavity. Closed drainage is used posteriorly and anteriorly as well.

Postoperative Care.—*Postoperatively* the patient's requirements demand attention to the following: (1) Prevention of shock. Shock may occur from loss of blood and loss of plasma which is greater after thoracic operation than others, anoxemia, or cardiac embarrassment. To prevent shock, frequent blood and plasma transfusions are used. (2) Anoxemia is minimized by prevention of tension pneumothorax or pleural fluid and avoidance of bronchial obstruction by forced coughing, little use of opiates, and aspiration of the bronchi if necessary. Oxygen is used routinely. (3) Cardiac embarrassment is prevented by avoiding tension pneumothorax, large pleural effusions, mediastinal shift, and flutter. (4) Prevention of infection. Penicillin is given intramuscularly every three hours in 100,000 unit dosage and streptomycin, 0.25 Gm., every six hours. Sulfadiazine is given for three days postoperatively up to 4 Gm. a day with sodium bicarbonate. Empyema as a postoperative complication is seen less often since surgeons have paid special attention to the closure of the bronchial stump. This is accomplished by using one row of silk sutures and if possible inversion of the end by first removing a cartilaginous ring. Complete expansion of the remaining lung to avoid dead space and atelectasis which also may predispose to empyema (q.v.) is an invariable requirement.

Complications and Sequelae.—These include postoperative hemorrhage, reopening of bronchial stump with resultant tension pneumothorax or mediastinal flutter, or, later, bronchopleural fistula with empyema, empyema without bronchopleural fistula, acute or chronic, and extension of the bronchiectasis to other lobes. The latter is thought to be a failure to get all of the diseased lung at the time of operation rather than extension of the process. This seems logical because of the slow development of the disease. However, it is true that the basal segments of the lungs are most frequently involved. If the dependent position is a factor, then recurrence may take place in the dependent portion of the remaining expanded lung.

Prognosis.—The prognosis is excellent in children and young adults and is not so good in the older group or those with advanced lesions. Even here, symptoms are ameliorated, although some cough persists. Since most cases are seen in children and young adults, the prognosis is excellent in over 75 per cent of the cases. The mortality for all groups combined is about 5 to 8 per cent.

THE MEDIASTINUM

The mediastinum is the space in the thorax between the two lungs. *In front* is the sternum and behind, the vertebral column. The superior part of the mediastinum and behind, the vertebral column. The superior part of the mediastinum

contains the aortic arch, the innominate artery, the left common carotid and subclavian arteries, the innominate veins, part of the superior vena cava, the trachea, the esophagus, the thoracic and right lymphatic ducts, the phrenic, the vagi, the cardiac and recurrent laryngeal nerves; immediately behind the sternum lies the thymus gland. Fortunately, injuries are rare, due to the adequate bony protection. Infections occur infrequently, the most common cause being a perforation of the esophagus through accident or forceful instrumentation. This results in a spread ing infection known as mediastinitis, which is usually serious and often fatal.

Congenital Anomalies

Before birth the lungs are small and occupy only the dorsal portions of the thorax, whereas the mediastinum is very broad. With the onset of breathing, the lungs expand and compress the anterior mediastinum. The superior mediastinum lies above the upper level of the fibrous pericardium; the inferior mediastinum which lies below the level is divided into the following: (1) Anterior, which lies in front of the pericardium and is bounded in front by the sternum, laterally by the pleurae, and posteriorly by the pericardium. It contains loose areolar tissue, lymph vessels and nodes, and branches of the internal mammary arteries. (2) Middle, containing the heart and the eight great vessels passing to and from the heart. (3) posterior which lies behind the pericardium and also extends downward below its level. The lower eight thoracic vertebrae bound it behind, the pericardium and diaphragm bound it in front. Sometimes communications exist between the two pleural spaces. This is said to be due to overencroachment of the lungs on the yielding anterior mediastinum which becomes compressed and absorbs or is a thin septum as exists in the dog. Such communications cause no symptoms as long as the two pleural spaces are normal. If disease or malformation is present in either lung, herniation may occur with encroachment on the opposite side. The treatment for such anomalies is surgical repair, using the pericardium to make a septum.

Injuries to the Mediastinum

The mediastinum may be injured directly by a crushing force which drives the sternum inward or by penetrating wounds made by bullets or other foreign bodies. In Chapter 18 we considered the effects of injuries to the heart and blood vessels. Earlier in this chapter we reviewed the causes and effects of mediastinal shift and mediastinal flutter. Hemorrhage into the mediastinum, effusion, or actual flooding with retained fluid from traumatic perforation of the esophagus or emphysema increase the pressure within the mediastinum. When this rises to above zero, the large veins will collapse and all the symptoms and signs of cardiac tamponade will ensue, because blood cannot enter the heart, leading to early cardiac inadequacy with a precipitous fall in blood pressure which is sudden and dramatic. Any injury to the mediastinum may be serious because of the increase in mediastinal pressure. As in increased pressure elsewhere, the rapidity of its development is important. Thus in

brain injury a sudden increase in intracranial pressure causes alarming symptoms and signs, whereas the slow rise in pressure due to intracranial neoplasms allows local adaptations. The same is true of mediastinal pressures. Ultimately, however, in either case inestimable symptoms result.

The entrance of air into the mediastinum is more difficult to understand than the presence of blood, exudates, or transudates. Air may reach the mediastinum by the following routes: (1) along the fascial planes of the neck, following injuries to the neck, thyroidectomy, especially in substernal goiters, thymectomy, and other neck surgery; (2) through a perforation of the trachea, lung, bronchus, or esophagus, either traumatically or as an accident in bronchoscopy or esophagoscopy, rarely following pneumonectomy and lobectomy; (3) from the retroperitoneal space due to injuries through the back entering a hollow viscus, gas-producing bacterial infections; (4) from the interstitial tissues of the lung, the result of a rupture of the alveoli and the production of interstitial emphysema of the lung following injuries to the chest, thoracotomy, artificial pneumothorax; increase in intrapulmonary pressure from straining with the glottis closed or from occlusion of the trachea or bronchi with cough, rarely spontaneous rupture of the alveoli; (5) passage from the pleural cavity to the mediastinum following injuries or surgery on the lungs or mediastinum; (6) rarely, if ever, by dissecting its way between parietal pleura and the chest wall or beneath the visceral pleura. The most common is by way of the interstitial tissues of the lung (4).

Air escapes from the mediastinum (1) into the subcutaneous and deep tissues of the neck, (2) through the diaphragm about the aorta and the esophagus to the retroperitoneal tissues, and (3) into the pleural cavities, perhaps along the connective tissue surrounding the blood vessels. The reverse is not true; that is, air will go from the mediastinum into the pleura, causing a tension pneumothorax; the reverse is almost never true. Tension pneumothorax does not cause mediastinal emphysema unless there is a hole in the mediastinal pleura due to actual injury or there is associated interstitial emphysema of the lung.

The symptoms and signs may be mild on small accumulations; when large, there are pain, subcutaneous emphysema, obliteration of cardiac dullness, all the signs of increased intramediastinal pressure, pneumothorax, and x-ray evidence of air in the mediastinum, pleura, retroperitoneal space, and subcutaneous tissues.

The treatment for accumulations in the mediastinum is first to relieve pressure and then try to eliminate the cause. In hemorrhage this is done simultaneously. Foreign bodies may also be removed at this time or later. Fluid is drained. Air is evacuated through an incision in the jugulum and the introduction of a sterile catheter or tube. Rarely the sternum is split to get complete evacuation. Tension pneumothorax is treated as previously outlined; sometimes with small amounts of air, no treatment is necessary.

Inflammations of the Mediastinum (Mediastinitis)

Anatomy

The fascial spaces on the floor of the mouth, in the neck, and in the mediastinum are important because they are the passageways for exudates and transudates upward and downward, forming almost a clear channel from the mandible down to the diaphragm. (See Fig. 232.)

The floor of the mouth contains three paired and one unpaired space. The former consists of the submental, sublingual, and submaxillary and the latter is a variable space or spaces between the extrinsic muscles of the tongue. These spaces are in relation to each other and to the parotid spaces by way of the posterior facial vein. Without the pharynx, the peritonsillar space is in close relationship with the pharyngomaxillary (parapharyngeal) and retropharyngeal space which in turn may lead an exudate into the retrovisceral compartment of the mediastinum.

An infection may start from an injury to the lower lip and travel into the submental, then the submaxillary space, along the intra-oral prolongation of the submaxillary gland, and along Wharton's duct into the sublingual fossa; from here, across the midline through the space of the extrinsic muscles of the tongue to the opposite sublingual and submaxillary spaces. This leads to great swelling of the floor of the mouth as seen in Ludwig's angina. This may lead to further extension as follows: to the parotid space by way of the posterior facial vein, from the parotid space to the neighboring parapharyngeal and retropharyngeal spaces, from here to the subtemporal fossae, and then to the pterygoid spaces which contain the pterygoid plexus of veins. These may be involved by a thrombophlebitis and cause an infection to extend into the cavernous sinus, producing a meningitis. Extension may be downward into the mediastinum by way of the retrovisceral compartment.

The neck is enclosed in a collar of fascia (fascia colli) attached above to the mandible, zygoma, mastoid process, and superior curved line of the occipital bone and below to the sternum and clavicles. It is divided into three compartments by two fascial partitions which cross from one side of the neck to the other: a posterior or vertebral containing the muscles which support the cervical vertebrae; a visceral or middle compartment containing the great vessels of the neck, the pharynx, esophagus, and thyroid gland; and an anterior containing the sternohyoid, sternothyroid, and sternomastoid muscles. Within the vertebral compartment a cold abscess arising from caries of the vertebrae may pass upward to the base of the skull or downward to the posterior mediastinum, whereas in the visceral compartment, infections from the mouth and pharynx and perforations of the esophagus may cause deep cervical abscesses or spread down to the mediastinum. The carotid sheaths which are simply lateral enclosures by the cervical fascia and lymph channels may act as pathways of communication.

Mediastinal compartments (Pearse) may be divided into retrovisceral, viscerovascular, and previsceral.

The *retrovisceral compartment* lies in front of the prevertebral fascia. Therefore, it is a potential space which lies betwen the vertebral fascia posteriorly and the pharynx and the esophagus anteriorly and extends from the base of the skull to the diaphragm. However, at the bifurcation of the trachea it sometimes blends together, forming a platform which may act as a barrier to the descent of exudates into the retrovisceral compartment which lies below this level. Below the diaphragm the retrovisceral space continues as the retroperitoneal space.

The *viscerovascular compartment* is divided into three parts: (1) *Pretracheal space* which extends from the larynx above to the bifurcation of the trachea below, anterior to the trachea and behind the thyroid gland. This space is rarely involved by infections of the floor of the mouth. (2) *Vascular* space which is simply the lateral prolongation of the fascia of the visceral compartment. It is a sheath for the carotid artery, jugular vein, and vagus nerve. Many observers do not believe that this offers a direct connection with the mediastinum. Others aver that it may form a potential

avenue for infection to descend. It has been stated that if you wish to find pus deep in the neck, you must first locate the carotid artery. A curved incision from the angle of the jaw to the symphysis will expose the submaxillary gland lying between the two bellies of the digastric muscle, as a sling. The anterior border of the sternocleidomastoid muscle is a sure guide to the carotid artery below the level of the hyoid bone, and the posterior belly of the digastric is a guide to the artery higher up. Even though pus does not actually descend down the sheath, it is certainly true that the sheath acts as a pathway upon which exudate and transudate may find its way downward, although it is probably true that pus rarely forms in the sheath itself. (3) Previsceral compartment which is the potential space or compartment anterior to the thyroid gland and posterior to the ribbon muscles of the neck (sternohyoid and sternothyroid). It is closed below by fascial attachments to the manubrium. Every surgeon encounters this space as he does a thyroidectomy, and no doubt he has observed the loose areolar tissue with which it is filled. These spaces are important in the study of infections of the mediastinum and the neck because they form the roads which exudates will follow just as the fascial spaces of the hand, lower abdominal wall, and other fascial planes determinate the routes of exudates and transudates.

Causes of Mediastinitis.—(1) Perforation. This may be caused by foreign bodies, by accidental wounds penetrating into the thorax, or by instrumentation in doing esophagoscopy in an attempt to remove a foreign body or dilate a stenosed or strictured esophagus. (2) Intrathoracic inflammations such as lung abscess, pericarditis, suppuration of the tracheobronchial lymph nodes, mediastinal empyema, pneumonia, and among rarer conditions, the fungus infections such as actinomycosis. (3) Very rarely extension of infection below the diaphragm upward as in the subdiaphragmatic abscess. (4) Rarer still, complications of scarlet fever, or other exanthematous fevers, influenza, and septicemia. (5) In the posterior compartment vertebral caries due to tuberculosis or tuberculous lymph nodes breaking down and forming an infection which descends into the mediastinum. (6) Among the more rare, syphilis which may be a very disabling disease, forming a diffuse fibrotic mass of tissue and actually occluding the venous return through the mediastinum. (7) A postoperative infection following tracheotomy, and thyroidectomy, pneumonectomy, lobectomy, the removal of mediastinal tumors, esophagectomy, etc.; also, in operations on the pericardium and osteomyelitis of the spine, infection may occur in the mediastinum. (8) Infections secondary to inflammations of the neck and floor of the mouth which have already been discussed.

Signs and Symptoms.—Symptoms and signs of mediastinitis may be extremely mild with a low-grade fever and very little pain. The leucocyte count may also be within normal limits. The more severe types, however, are easily recognized because of pressure symptoms which give rise to nerve irritation and cause severe pain and tenderness in the chest and sternal pain radiating to both shoulders. In anterior mediastinitis the pain and tenderness are more localized in the sternal area. If there is an accumulation of fluid, whether it be transudate or exudate, there may be interference with venous return, and all the symptoms and signs of mediastinal pressure which have been discussed

under Injuries to Mediastinum and which will be discussed again under Mediastinal Tumors and Cysts may be present.

The x-ray offers considerable help in making the diagnosis because it may show a widening and a distortion of the mediastinal shadow. A lateral picture may fail to reveal the clear space which is ordinarily, but not invariably, demonstrated in the posterior mediastinum. Of course, if there has been a perforation of the esophagus, there will be air in the retrovisceral compartment which may be ascertained by x-ray examination. In addition there may be mediastinal emphysema of great magnitude. There may also be subcutaneous emphysema. Usually the diagnosis will not be difficult if a careful history is taken and if the lesion is suspected.

Treatment.—The treatment of mediastinitis requires immediate operation and will be considered in relation to the various causes of the disease. Before discussing this phase it should be stated that the mediastinum is indeed a closed space and, therefore, it would be unwise to wait for localization in the ordinary sense of the term because it is already localized anatomically. We have learned this principle in discussing infections of fascial spaces of the hand, the distal anterior closed spaces of the finger, and the ischiorectal space. This, then, is another example of an anatomical localization of infection which permits early drainage. Mediastinitis due to perforation of the esophagus may be prevented if the lesion is recognized and prompt suture of the esophagus is performed. A small perforation need not be sutured; that is perforations which are caused by a chicken bone or safety pin. However, large tears or injuries by the esophagoscope or penetrating wounds demand immediate suture. This is best accomplished by making an incision posteriorly, lateral to the vertebral column, and over the site of the perforation. An extrapleural approach is desirable. Sometimes, however, transpleural approach may be necessary. The esophagus is sutured and a soft drainage tube is placed into the mediastinum extrapleurally; then an intranasal tube is inserted so that feeding may be continued without using the esophagus.

Retropharyngeal abscess may be drained by an incision on the posterior wall of the pharynx. This is a common lesion and early drainage is indicated for two reasons: (1) so that perforation does not occur spontaneously, permitting aspiration of pus during sleep; this may be followed by a lung abscess or a disseminating pneumonitis (2) if the abscess is pulsating or if it has been present for some considerable time, a weakening of the wall of the carotid artery may result; this is important, as actually the pulsating abscess has caused a necrosis by pressure; then, when this pressure is suddenly released, severe or even fatal hemorrhage may result. Therefore, in such cases it has been our policy to isolate the common carotid artery first and place a ligature loosely around it. If bleeding does not occur, this need not be tied. It is left in place for twenty-four hours.

Mediastinitis due to infections in the neck or from many other causes in which the superior mediastinum is involved may be treated by an incision parallel and anterior to the sternomastoid muscle in the lower part of the neck. The great vessels are retracted posteriorly, the thyroid gland medially. It may be necessary to ligate the middle thyroid vein and inferior thyroid artery to mobilize the lateral lobe of the thyroid gland better. This is the same route that we use in removing esophageal diverticulum. This gives us a good approach and may be done bilaterally if necessary. Through this opening a foreign body may be removed or a perforation may be closed if it is large. If it is a small perforation with infection, drainage is instituted and a nasal feeding tube is passed so that the esophagus may be put at rest. This incision also permits drainage of the pretracheal space. However, the previsceral compartment is better drained through an ordinary thyroidectomy incision. Indeed, this area is sometimes infected following thyroidectomy and the incision is partially reopened.

A word should be said concerning drainage of the posterior mediastinum with abscess. If it is below the sixth dorsal vertebra, a posterior, extrapleural approach is best. The incision is made lateral to the vertebral column and the overlying ribs are removed subperiosteally for a distance of about two or three inches. The parietal pleura and endothoracic fascia are reflected anteriorly and thereby the pleura is not transgressed. Drainage tubes are placed down on each side of the infection.

The anterior mediastinum may be entered through a peristernal incision, very much like that which is made to enter the pericardium. Great care, however, is exercised not to violate either the pericardium or pleura. Usually this is not as difficult as it may sound, because the infection has thrown up barriers and the abscess cavity is entered rather easily. However, if either the pleura or the pericardium has been injured, it should be sutured immediately after irrigation has been done. Sometimes it is necessary to rongeur away a part of the sternum in order to reach this space.

In addition to the local treatment of mediastinitis, systemic treatment is always necessary. This consists of careful attention to water balance by intravenous route or by the Levine tube, blood transfusions where indicated, penicillin, and the sulfonamides, intravenously or through tubes. The high mortality of mediastinitis has been greatly reduced by early diagnosis and proper treatment.

Mediastinal Tumors and Cysts

Since the advent of modern chest surgery, hundreds of cases of mediastinal tumors have been reported. Heuer believes the origin of dermoids and teratomas to be due to ectodermal displacements or abnormal cells of branchiogenic origin drawn into the chest by the descent

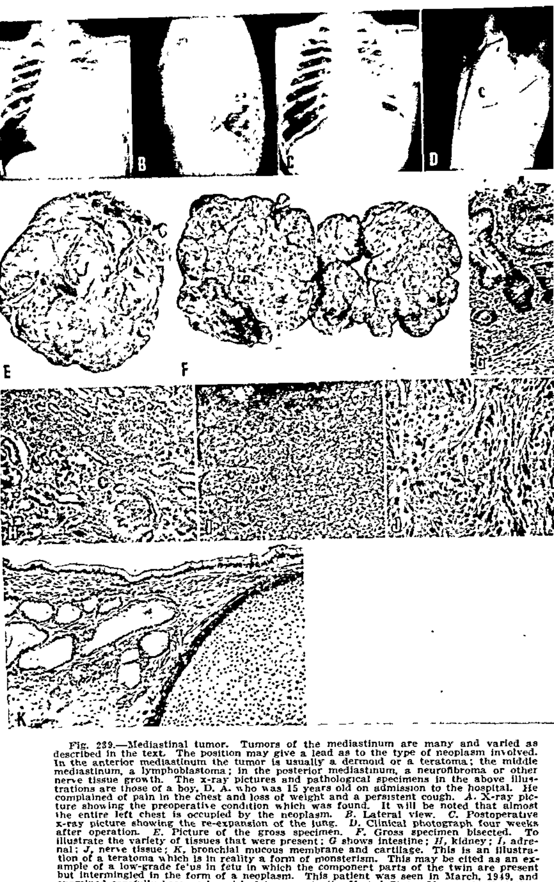


Fig. 239.—Mediastinal tumor. Tumors of the mediastinum are many and varied as described in the text. The position may give a lead as to the type of neoplasm involved. In the anterior mediastinum the tumor is usually a dermoid or a teratoma; the middle mediastinum, a lymphoblastoma; in the posterior mediastinum, a neurofibroma or other nerve tissue growth. The x-ray pictures and pathological specimens in the above illustrations are those of a boy, D. A. who was 15 years old on admission to the hospital. He complained of pain in the chest and loss of weight and a persistent cough. *A*. X-ray picture showing the preoperative condition which was found. It will be noted that almost the entire left chest is occupied by the neoplasm. *B*. Lateral view. *C*. Postoperative x-ray picture showing the re-expansion of the lung. *D*. Clinical photograph four weeks after operation. *E*. Picture of the gross specimen. *F*. Gross specimen bisected. To illustrate the variety of tissues that were present; *G* shows intestine; *H*, kidney; *I*, adrenal; *J*, nerve tissue; *K*, bronchial mucous membrane and cartilage. This is an illustration of a teratoma which is in reality a form of monsterism. This may be cited as an example of a low-grade fetus in fetu in which the component parts of the twin are present but intermingled in the form of a neoplasm. This patient was seen in March, 1949, and examined carefully because he wished to serve in the United States Navy. At that time his general condition was excellent and the x-ray film showed no return of the neoplasm. (From Berman, J. K., Powell, J. P., and Hennessey, P. C.: Am. J. Surg. 74: 205, 1947.

of the heart. Many other theories have been advanced to explain the presence of teratomas and dermoids which are perhaps the most common variety of mediastinal tumor.

Teratology is a subdivision of embryology that deals with abnormal development and its end products—anomalies. While it is certainly true that not all teratomas are examples of monsters, yet a great proportion probably are. Identical or duplicate twins are really an example of teratoma. They develop from a single egg, whereby each member acquires precisely the same chromosomal heritage and hence the same genetic constitution. If they are the same size and completely separate, they form two normal individuals. Identical twins may be a double monster when conjoined and this connection may take place anywhere in the body. If they are joined in the thorax, they are called thoracopagus, sternopagus, or xiphopagus. Sometimes they are not the same size and in such instances the larger is known as the autosite, the smaller the parasite. The latter may be almost a completely developed included twin, fetus in fetu, which grades down into the teratomas that contain disorderly assortments of tissues or organs.

Other theories include the idea that there is an arrest of certain blastomeres which subsequently undergo a partial fulfillment of their primitive developmental potentialities, Cohnheim's theory of cell rests which later for unknown reasons begin to grow, and, last, the unproved concept of parthenogenesis of ovarian eggs.

Types of Mediastinal Tumors.—The mediastinum is a fertile ground for tumors and cysts. This is due to the complexity of its development and its component tissues. The following is a useful, but by no means exhaustive, classification of these abnormalities:

A. Neoplasms and hyperplasias of the thyroid and parathyroid glands
B. Neoplasms and hyperplasias of the thymus
C. Neoplasms of nervous tissue
    1. Sympathicoblastoma
    2. Hour-glass tumors
    3. Neurofibroma, neurilemmoma, neuroma ganglionare
D. Connective tissue neoplasms
    1. Lipoma
    2. Fibroma
    3. Chondroma
    4. Myxoma
    5. Xanthoma
    6. Sarcoma
E. Tracheal and esophageal neoplasms
F. Tumors of lymph nodes
    1. Acute inflammations, tuberculosis (cold abscess)
    2. Lymphoblastomas
        (a) Hodgkin's disease
        (b) Leucemia
        (c) Lymphosarcoma
    3. Endothelioma
    4. Metastatic carcinoma

G. Cystic tumors
   1. Epidermoid
   2. Bronchiogenic
   3. Gastrogenic
   4. Lymphangiomatous
   5. Venous
   6. Pericardial
   7. Pleural
   8. Mixed (dermoid)
   9. Echinococcus
   10. Branchial
   11. Duplication of esophagus
   12. Undetermined

H. Vascular tumors
   1. Aneurysm of aorta
   2. Aneurysm of heart

I. Tumors of pericardium and heart, pericardial cysts, diverticula of pericardium

Symptoms and Signs.—The behavior of mediastinal tumors and cysts is erratic and variable. They may grow or remain quiescent for years. Most observers believe that they grow as the child grows and that they cease growing after maturity, barring complications which would increase their size, such as trauma, infection, or malignant change. Malignant degeneration is uncommon. Heuer states that the largest tumor reported was 15 × 11 × 9 cm. (Smith and Stone). Schneider's case was 45 cm. In sixty cases of dermoids and teratomas, only seven were the latter. Mediastinal tumors seem to grow as the child grows. We have reported one whose size is perhaps one of the largest on record, measuring 20¾ × 20½ × 9 cm. in a body 14 years of age. (See Fig. 239.)

Other types of neoplasms will cause symptoms, depending on the rapidity of their growth, their position, and type.

The symptoms and signs are due mainly to the increase in mediastinal pressure but also to displacements of organs. The former interferes with the return of blood through the superior vena cava and may cause cyanosis, orthopnea, dilation of the superficial veins of the thorax, pulmonary edema, and pleural and pericardial effusions. If the obstruction is above the azygos vein, the symptoms are less severe. If below and pressure is great, there may be subcutaneous edema of the head, neck, and upper part of the thorax, headache, vertigo, deafness, epistaxis, tinnitus, and even convulsions.

Posterior mediastinal tumors such as ganglioneuromas are apt to interfere with the function of the cervical sympathetics, producing Horner's syndrome.

By far the most common symptom of dermoids and teratomas is the persistent cough with or without hemoptysis and dyspnea, which is especially pronounced on the slightest exertion. There may also be dysphagia or regurgitation, hematemesis, and recurrent attacks of asthma or pneumonia. Occasionally a patient with a mediastinal dermoid will cough up hair. This symptom is diagnostic.

Fig. 240.—X-ray picture of a child, M. C., 4 years of age, with a mediastinal tumor involving the anterior mediastinum. This child was admitted to the hospital because she had swallowed a watch chain. Routine films disclosed the tumor mass. *A* and *B*. Preoperative film in the posteroanterior and lateral positions. *C*. Postoperative film taken nine days after surgery. The growth proved to be a teratoma. A checkup made in May, 1949, showed the child to be well and in good health two and one-half years after surgery.

Fig. 241.—X-ray films illustrating mediastinal tumor of the posterior mediastinum. The patient, a woman 31 years of age, complained of pain in the back which radiated anteriorly and into the epigastrium. *A.* Postteroanterior view of the neoplasm as it extends into the left thoracic cavity. *B.* Lateral view showing the tumor mass to be posterior and to lie over the vertebral column. *C.* Postoperative film after the removal of the growth which proved to be a neurofibroma of the hour-glass variety. Patient has remained well.

The size of the growth usually displaces the lung and heart so that there is absolute flatness on percussion, and heart sounds and breath sounds are absent or only faintly heard over the affected side. Sometimes there are no symptoms and the growth is discovered by routine *x-ray examination as in many of our cases.*

Diagnosis and Treatment.—The diagnosis of mediastinal growths *is made by the history, physical examination,* x-ray *films* made *in the* anteroposterior, lateral, and oblique positions, fluoroscopic studies, bronchography, partial pneumothorax, and thoracentesis. Roentgenographic studies are indispensable not only for diagnosis, but also for position and behavior fluoroscopically. In general, the roentgenologist will note the following characteristics:

1. Position. If in the anterior mediastinum the tumor is usually a dermoid or teratoma; the middle mediastinum, a lymphoblastoma; the posterior mediastinum, a neurofibroma or other nerve tissue growth. *Therefore, the position is a clue to diagnosis. Moreover, it is important* in determining the surgical approach. If it is cervical and retrosternal, presenting at the base of the neck, the cervical route or the cervical with division or resection of the superior portion of the sternum is the most direct avenue to the growth. If retrosternal, not extending beyond the mediastinum, access to the growth may be obtained through a trap door incision, transverse sternotomy, or median and vertical *sternotomy which may be superior or inferior or which may traverse the* entire length of the sternum. If the neoplasm is mediastinothoracic, extending into either thoracic cavity, or if it is in a lateral thoracic position, a transpleural approach is best. Posterior neoplasms may usually be removed extrapleurally by resecting the overlying ribs; sometimes laminectomy must be done in removing hourglass tumors.

2. The presence of shadows indicating teeth or bone leads to the diagnosis of dermoid or teratoma.

3. The spine may show evidence of compression. This, with the larger mediastinal shadow, is characteristic of an hourglass tumor.

4. The mass may pulsate. This is best observed fluoroscopically or by the roentgenokymograph and if present, together with a positive blood test for syphilis, or the presence of arteriosclerosis, an aneurysm is the most likely diagnosis.

5. The effect of x-ray treatment on *the size of the mass may help* distinguish between different types of lymph node involvement and may also locate the enlargement in the middle rather than in the anterior mediastinum—a distinction not always easy. Lymphoblastomas are sensitive to x-ray. Leucosarcomas in children regress after roentgen therapy and then later emerge with a full-blown *leucemia. Benign* tumors are not usually radiosensitive.

Bronchography will help in the detection of primary lung neoplasms with mediastinal metastasis and will indicate the site and degree of

bronchial compression from mediastinal growths. Partial artificial pneumothorax may help reveal the exact position of the mass, its fixation, density, and regularity, especially if studied fluoroscopically. Thoracentesis helps rule out encapsulated empyemas, particularly interlobar types. This is especially true now since the use of penicillin locally has become popular. A localized empyema may be sterilized and converted into an inflammatory cyst.

TRACHEOESOPHAGEAL FISTULA

Esophagotracheobronchial fistula may be congenital or acquired. Since most of these fistulae are primarily esophageal problems, they will be considered in Chapter 20 under the alimentary system. We are interested here in those anomalies and acquired defects of the esophagus which result in fistulae.

The *congenital defects* of the esophagus occur once in 2,500 births and may result in: (1) Its complete absence. (2) A blind upper and lower end. (3) Tracheoesophageal fistula, which may be present in three ways: (a) the upper end of the esophagus communicates with the esophagus, the lower segment is blind; this is a rare type; (b) the upper segment is blind and the lower segment communicates with the trachea; this is the most common type; (c) both the upper and lower segments communicate with the trachea; this is also a rare type. The diagnosis of congenital tracheoesophageal fistula is not difficult. In all types there is a large amount of mucus present at birth and all attempts at feeding result in strangling, coughing, and cyanosis. A catheter will not pass into the stomach and in type 3 (a) it goes into the trachea and Lipiodol swallowed goes immediately into the tracheobronchial tree and may be seen fluoroscopically. There is no gas in the stomach or intestines. Type 3 (b) presents the most common picture. A catheter will not pass. The stomach and intestines are greatly distended; Lipiodol is observed fluoroscopically to descend to the end of the upper segment and is then regurgitated and then aspirated, and from the trachea it may pass into the esophagus. Type 3 (c) may not permit the catheter to pass; gas will be present in the intestines and Lipiodol will go into the trachea and lower esophagus at the same time. Rarely an opening may be present at this juncture creating a tracheoesophageopleural fistula. Repair is accomplished through an extrapleural approach on the right side, posteriorly, with resection of one or more ribs. The fistula is ligated and divided and direct anastomosis is done. In type 3 (a) as well as in other types the distance between the two ends may be so great that anastomosis cannot be done without too much tension. In such cases the upper end is brought out through the neck and the lower end through the upper abdomen. Later a skin esophagus is made, uniting the two ends, or the stomach is mobilized by a transpleural approach and brought up to the neck.

Acquired fistulae between the esophagus and tracheobronchial tree may be due to: (1) malignant disease of the esophagus, (2) infections of the esophagus, trachea, or pleura due to tuberculosis, which may also be primary in the nodes, causing caseation, syphilis, fungus infections, suppurative esophagitis, and nontuberculous empyema, (3) traumatic injuries of the esophagus, (4) esophageal diverticula, (5) esophagomalacia seen as a terminal event in cerebral disease, as a result of digestion by gastric contents. The symptoms and signs are dysphagia and cough. Diagnosis is made by x-ray examination, bronchoscopy, and esophagoscopy. The treatment varies with the cause. Small fistulae may be treated by chemical cauterization through the bronchoscope; larger ones must be closed, usually by a transpleural approach, although traumatic types may be treated by an extrapleural operation. In empyema, primary closure or prolonged esophageal rest by nasal tube feeding and adequate drainage of the empyema is done. In carcinoma very little can be done because the lesion has already advanced too far, although a combined esophagectomy and pneumonectomy may be tried in some cases. Gastrostomy is done for feeding.

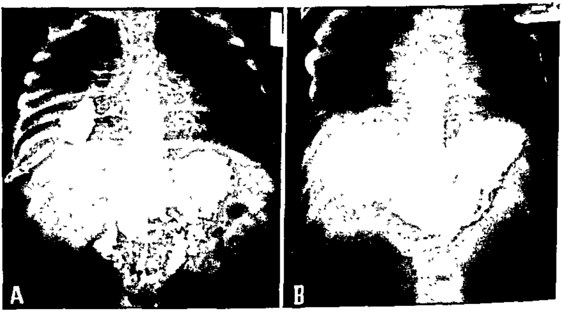


Fig. 242.—Sometimes pleural and mediastinal diseases are combined due to communications between the two compartments. *A*. X-ray picture showing a bronchoesophagopleural fistula. Iodized oil was injected through the thoracotomy wound. *B*. Roentgenogram showing the esophagus after a barium meal. Fistulae are closed and all wounds have healed.

D. A., a boy 23 months of age, was admitted to the hospital in 1941. His aunt, who gave the history, stated that the child had been desperately sick since birth and that everything he ate ran out through a tube which had been placed in the right chest. This had been done by the family physician because of an empyema. However, upon opening the chest cavity the physician noted that milk was present within the thorax. At the same time he noted that when milk was given by mouth, it was found to run *out of the* tube which had been placed within the thorax. The physician then did a gastrostomy for feeding. But when milk was injected into the gastrostomy tube, *it found* its way up and made the child cough. It was obvious that there was a connection between the esophagus and the bronchial tree and the pleural space.

The patient was operated upon in stages; the bronchoesophageal fistula was separated both openings were closed, and then the empyema cavity was obliterated by parietal decortication and muscle flap closure. The patient has remained well. (After Berman, J. K., and Walters, C. E.: Ann Surg. 117: 100, 1943.)

DIAPHRAGMATIC HERNIA

The subject of diaphragmatic hernia could be considered as a part of the discussion on the abdomen or on the thorax because it forms a floor of the latter and the roof of the former. However, it is perhaps best that we discuss it in connection with disease of the thorax since thoracic symptoms are prominent, and in most types of diaphragmatic hernia, the thoracic approach is desirable in the surgical correction of the defect. However, the abdominal route is favored by many and both may be used in a combined thoracic and abdominal incision.

Embryology

The diaphragm is a complex structure and is derived embryologically from several anlage. The first of these is the transverse septum and the fused dorsal mesentery. This gives rise to the anterior, lateral, and the central parts of the diaphragm, thereby forming the greater portion of this structure in the adult. The dorsal mesentery and the mesoderm which is derived from the receding wolffian body, together with the pleuro peritoneal membrane, which is derived from the pulmonary ridge, fuse to form the posterolateral portion of the diaphragm. The exact amount of muscle which is derived from each anlage is variable. The mesodermal cells from the receding wolffian body go to form the right and left crura of the diaphragm. It is probable that the dorsal mesentery gives rise to the posterior and central portions which contain the esophageal hiatus. The pleuroperitoneal membrane grows anteriorly, closing the remaining opening; namely, the pleuroperitoneal hiatus between the peritoneal and pleural cavities. This occurs by fusion with the transverse septum and forms the lateral portion of the diaphragm. Another classification as to the embryological derivation of the diaphragm is as follows: (1) its ventral pericardial portion from the septum trans versum, (2) its lateral portions from the pleuroperitoneal membranes, (3) its margins derivatives from the body wall, (4) a medial dorsal portion from the dorsal mesentery. An understanding of the embryological development will make clear the types of diaphragmatic hernia which may be encountered.

Hernia is seldom seen on the right side due to the broad attachment of the liver. On the left side the surgeon encounters the stomach, spleen, splenic flexure of the colon, and the left lobe of the liver.

Types of Diaphragmatic Hernia

(1) Subcostosternal diaphragmatic hernia. This variety goes through an area which should have been covered by a derivative of the septum transversum. It lies directly posterior to the sternum and has been called hernia through the foramen of Morgagni and through Larrey's fissure or space and substernal, retrosternal, parasternal, or anterior diaphragmatic hernia. The fissures or spaces occur on either side of the midline. This type is rare, and we have had one case. (2) Esophageal hernia through the esophageal hiatus. This type is most common in adults. (3) Dome hernia which is an opening which occurs at the highest point of the diaphragm which seemingly is due to lack of fusion between the septum transversum and the pleuroperitoneal membrane derivatives as well as the derivatives of the mesentery. (4) Pleuroperitoneal hiatus hernia. This is seen most commonly on the left side, although we have had two cases on the right side.

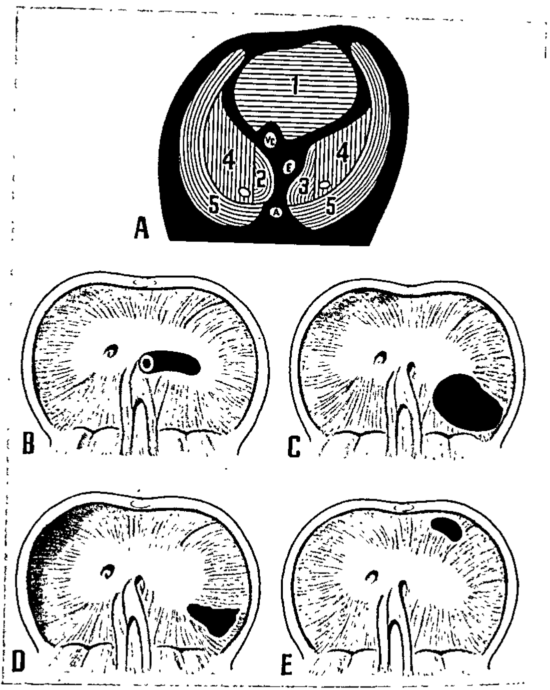


Fig. 243.—Congenital types of diaphragmatic hernia. *A*. Diagram which has been modified showing the origin of the diaphragm. (After Berman, J. K., and Ballenger, F.: Quart. Bull. Indiana Univ. M. Center 4: 36, 1942.) *1*, Septum transversum; *2* and *3*, derivatives of mesentery; *4*, derivatives of pleuroperitoneal membrane; *5*, parts derived from the body wall, *VC*, vena cava, *E*, esophagus; *A*, aorta. (From Prentiss, C. W.: Textbook of Embryology, Philadelphia, 1915, W. B. Saunders Co.)

The lower diagrams are modified from Harrington, S. W.: Western J. Surg., Obst., and Gynec. 44: 255, 1936.) *B*. Esophageal hiatus hernia. *C*. Congenital absence which may be due to the lack of development of derivatives of the mesentery, the pleuroperitoneal membrane, and body wall (transversalis and rectus muscles). More common on the left. *D*. Pleuroperitoneal hiatus hernia which is due to the absence of the derivatives of the pleuroperitoneal membrane. More common on the left perhaps because of the liver. *E*. Parasternal hernias are more common on the right than on the left, perhaps because of the larger attachment of the pericardium on the left. Since the septum transversum forms this part of the diaphragm, it is difficult to explain the hernia on a strict embryological fusion or absence basis. It may be due to a defect in the structure of the diaphragm or a faulty attachment of the right and middle leaflet of the diaphragm to the sternum and costal cartilages.

In addition to the foregoing classifications, there may be a congenital absence of half of the diaphragm. *Also a thoracic stomach, with* or without a short esophagus, may resemble hernia due to the development of the stomach above the diaphragm. Lastly, eventration, or a high diaphragm, may resemble a diaphragmatic hernia. In this case, the diaphragm is immobile and is fixed to a high point, permitting the stomach to lie at an extremely high level. Very rarely an inflammatory necrosis may occur. One other classification should be mentioned and this is congenital or acquired. Of the acquired types, trauma may play an important role. However, nontraumatic types of hernia are common, especially through the esophageal hiatus.

Symptoms and signs of diaphragmatic hernia will vary with the type or variety. Let us now discuss the symptoms and signs of each variety as given in our outline and then we may consider the methods of treatment.

One is the unusual congenital type of hernia known as the *subcostosternal diaphragmatic hernia.* It is also known as the substernal, retrosternal, parasternal, or anterior diaphragmatic hernia. Some authorities do not regard it as a congenital hernia and prefer to classify it as acquired. It is true that it would be difficult, on the basis of our embryological discussion, to account for the particular faulty fusion which may occur, since this part of the diaphragm is all formed by the septum transversum and no other structure. Therefore, there is an argument in favor of its acquired nature. However, the hernial opening is very constant and the hernial sac has a constant relation to the round and falciform ligaments of the liver. Also, the sac frequently protrudes in the right thoracic cavity at the same point as the cardiophrenic angle. Also in connection with this type of hernia, the abdominal cavity does close off from the peritoneal cavity as is evidenced by the presence of a peritoneal layer or sac.

Only two types of diaphragmatic hernia consistently have a sac, and this is important to the surgeon in effecting a cure. One is the hernia under discussion, namely, the subcostosternal hernia, and the other is the esophageal hiatus hernia which is clearly an acquired type, although in the latter, too, there must be a congenital defect or the hernia would not occur.

Symptoms and signs of the subcostosternal hernia will depend upon the abdominal viscera that have protruded and the impairment of respiration. In most types of diaphragmatic hernia there is an interference of respiration, producing dyspnea and cough, and there may be interference with intestinal functions producing symptoms and signs of intestinal obstruction. X-ray examination usually reveals the diagnosis very clearly. Fluoroscopic examination also helps to differentiate the particular variety of hernia which is being discussed. If there is *no protruding* bowel, but simply some omentum, diagnosis is more difficult and

sometimes cannot be made preoperatively. The omentum gives no abdominal symptoms, but there is interference with respiration. Sometimes this type of hernia may be mistaken for a mediastinal tumor.

Treatment for this type of hernia is surgical and the approach is perhaps easier through the abdomen because the opening is very accessible. Rarely there is also a congenital deformity of the thorax and a combined operation may be necessary; namely, both thoracic and abdominal incision. For this reason in all types of diaphragmatic hernia it is best to work under endotracheal anesthesia so that respiration may be continued when the chest is open. Usually the hernia sac is easily identified and may be tied off and the opening closed by overlapping edges of the diaphragm after the abdominal viscera have been replaced. If there is an associated anomaly of the chest, this may be taken care of in accordance with the principles laid down previously in this chapter.

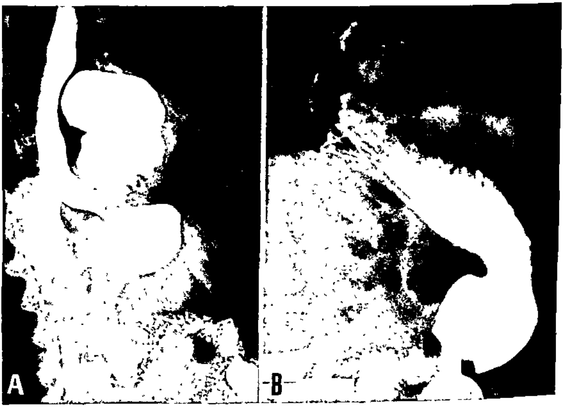


Fig. 244.—Esophageal hiatus hernia. Perhaps the most common of all acquired types of diaphragmatic hernia is illustrated by this case of a woman, M. H., who came to the hospital complaining of epigastric pain, regurgitation of food, and shortness of breath. *A*. Preoperative film in a slightly oblique view. This shows an esophageal hernia which has been popularly termed "upside-down stomach." It will be noted that the esophagus enters the stomach below the diaphragm, that the fundus of the stomach and most of the body of the stomach are within the pleural cavity, and that the pylorus is again below the diaphragm. *B*. Postoperative film showing the structures returned to their normal position. This operation was performed through the eighth intercostal space. The phrenic nerve was crushed and the hernial sac identified and opened. Careful exploration failed to reveal any ulcer or new growth or other abnormality at the site of the constriction. The sac was imbricated very much as in the method of treating a sliding hernia or a direct hernia by tiers of purse-string sutures. The diaphragm was then repaired, using interrupted silk sutures. A few of the sutures were passed through the serosa of the fundus of the stomach to prevent a re-ascent of the stomach into the pleural cavity. (Case referred by Dr. L. F. Bloemker.)

(2) *Esophageal hiatus hernia* is considered next because it is the only other variety of diaphragmatic hernia having a sac. The esophageal hiatus hernia, as its name implies, is a herniation through the esophageal opening. It is the most common type of diaphragmatic hernia occurring in adult life. Its symptoms and signs are so bizarre that it has been known as the masquerader of the upper abdomen, leading to erroneous diagnosis because it may simulate almost any disease in the upper abdomen. Furthermore, it is important because of some of its complications, such as intestinal obstruction, ulceration of the stomach, incarceration of the stomach, ulceration and fibrosis at the cardia, and severe secondary anemia. The cause of the latter is not known, although gastric bleeding is thought to be a factor, but it is an observed fact.

The symptoms and signs of esophageal hiatus hernia may vary from practically none at all to those of pain, abdominal distress, vomiting, gaseous eructation, dyspnea, hemorrhage, severe weakness with anemia, and the various symptoms and signs leading to the suspicion of heart disease. In fact, many cases have been diagnosed as angina pectoris before the true nature of the condition was discovered. The diagnosis is made, of course, by the use of the fluoroscope and x-ray films. Esophagoscopic examination may be used to rule out lesions within the esophagus.

Some patients require no treatment at all; others require weight reduction so that they may have more room in the abdomen and less pressure upon the diaphragm. A third group requires surgery because of a large opening or complications such as incarceration or ulcer of the stomach. Whenever a third or more of the stomach is involved, there will be abdominal or thoracic distress and surgery is definitely indicated. The types of hernia that are found at operation are as follows: (1) the esophagus maintains its attachment to the diaphragm and the cardiac end of the stomach herniates alongside the esophagus. This is called para-esophageal hernia and is present in 20 per cent of the cases. (2) The esophagus is shortened and retracted, but it is long enough to reach the diaphragm by traction. This type constitutes about 70 per cent of the cases. These are usually large hernias and they are very difficult to correct because an opening must be left after surgery and the stomach and lower part of the esophagus are pulled above the diaphragm by the shortened esophagus. Fixation of these structures is difficult. (3) Congenitally short esophagus with thoracic stomach. This may also include cicatricial contractions of the esophagus. Treatment may be instituted by abdominal or thoracic approach. Harrington prefers the former. We have used the thoracic approach with great satisfaction. The phrenic nerve is temporarily interrupted by the injection of Novacain and rarely is it necessary to interrupt the phrenic nerve permanently. The esophagus is mobilized for a short distance and in congenitally short esophagus it is mobilized throughout its lower two-thirds so that the stomach may be returned to the abdomen. Perhaps in the type in which there is congenitally short esophagus this may be necessary so that the dia-

phragm will come up high enough to lie above the stomach. Also in patients who cannot stand surgery, phrenicotomy done under local anesthesia is a satisfactory method of palliation. However, this is not a common procedure in the treatment of esophageal hiatus hernia. The repair must be carried out very much like herniorrhaphy elsewhere; namely, the sac must be identified and separated, the stomach returned to the abdomen, the sac imbricated and partially removed. The sac is usually attached to the serosa of the stomach very much like a sliding hernia and therefore we prefer separating and imbricating it. After the sac has been obliterated, the hiatus is closed tight around the esophagus. In order to avoid closing it too tight, a fairly large esophageal tube is introduced in the esophagus and closure is made around this tube.

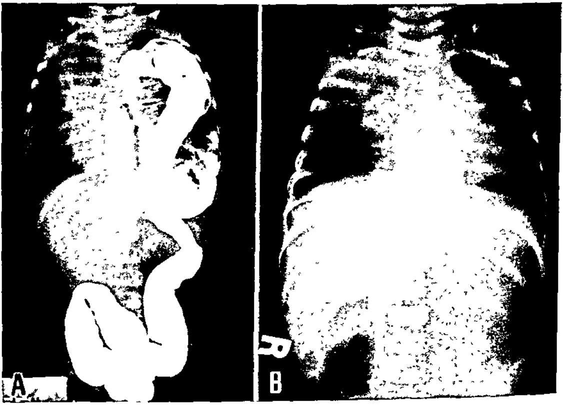


Fig 245—Pleuroperitoneal hiatus hernia. Congenital diaphragmatic hernia seen in a baby girl, S. F., 9 months old. *A*. Preoperative x-ray picture showing loops of bowel in the left half of the thoracic cage and dextrocardia due to the pressure of the intestines on the mediastinum, pushing the entire mediastinum to the right. *B*. Postoperative x-ray picture showing the lung to be expanded and the heart returned to the normal position. This case illustrates a left pleuroperitoneal hiatus hernia. The child has remained in good health. The congenital types of hernia are better repaired from below in general, particularly in the newborn. In older children and in adults the transthoracic route is by far superior in our experience.

Sutures are placed on both sides of the esophagus if the left crus is well developed at its muscular end. If not, it may be better to open the diaphragm anterolaterally and move the esophagus into a more anterior and lateral position before closing on each side. The esophageal hiatus should not be so tight that the forefinger cannot be inserted.

After imbrication of the sac and closure of the defect in the diaphragm, the mediastinal pleura is closed with interrupted silk sutures.

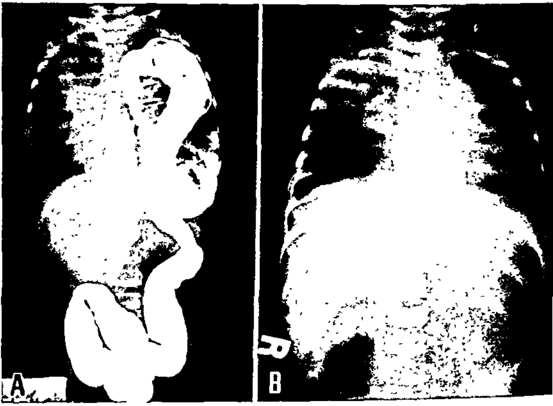
In some cases of very large hernias, a counter incision may be made in the diaphragm laterally, the herniated viscera delivered through this incision, and then the sac imbricated and the hiatus narrowed. Last, the incision in the diaphragm is closed. Fascia lata grafts may be used in extremely large defects. Recurrences are uncommon but do occur because the hiatus cannot be completely closed as in other types of diaphragmatic hernia.

Congenital types of hernia consist of *dome hernia, pleuroperitoneal hiatus hernia, congenital absence of half of the diaphragm* (which is usually within the posterior portion in the left side but may also be on the right), and those through the foramen of Morgagni or the subcostosternal type which we have already discussed.

Dome hernia is uncommon. Even its method of occurrence is not clearly understood. Since this occurs at the highest point on the diaphragm, it is not difficult to repair through the thorax. There is no sac; the commonness with which the abdominal viscera protrude is well known. It should be repaired through a thoracic incision in older children but not in infants because an abdominal approach at this high point would be extremely difficult. We have seen two of these and they have been repaired through the thorax with good results.

Pleuroperitoneal hernia is also a congenital type of hernia and may occur on either the left or right side. It is more common on the left, and on this side it is more conducive to the causation of symptoms. It does occur rarely on the right. We have seen three such cases. In two instances the liver had pushed up into the thoracic cavity to some extent. In one case, a loop of transverse colon had insinuated itself between the liver and the diaphragm and had pushed itself into the thorax, causing an obstruction. Since this type of hernia is a true structural deficiency, we find many associated anomalies, chiefly a failure of rotation of the right colon, but there may be many other anomalies. Protrusions through this type of hernia bring the abdominal viscera into direct contact with those of the thorax because there is no sac. Sometimes there is a little bit of loose areolar tissue which resembles peritoneum and this may be confusing, because it leads nowhere and it will be a waste of time to attempt to identify a sac in this particular type of hernia. Here, again, the phrenic nerve does not need to be crushed or divided, or permanently interrupted It may be temporarily paralyzed by using Novocain, but even this may not be necessary. We have used the thoracic approach in older children and an abdominal incision in the newborn or infant. The chief consideration in the care of such a hernia in an infant is the increase in the intra-abdominal pressure which occurs after it has been repaired. Very often when the contents of the hernia have been reduced there is not enough room in the abdomen to hold the returned viscera, and for

phragm will come up high enough to lie above the stomach. Also in patients who cannot stand surgery, phrenicotomy done under local anesthesia is a satisfactory method of palliation. However, this is not a common procedure in the treatment of esophageal hiatus hernia. The repair must be carried out very much like herniorrhaphy elsewhere; namely, the sac must be identified and separated, the stomach returned to the abdomen, the sac imbricated and partially removed. The sac is usually attached to the serosa of the stomach very much like a sliding hernia and therefore we prefer separating and imbricating it. After the sac has been obliterated, the hiatus is closed tight around the esophagus. In order to avoid closing it too tight, a fairly large esophageal tube is introduced in the esophagus and closure is made around this tube.



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Sutures are placed on both sides of the esophagus if the left crus is well developed at its muscular end. If not, it may be better to open the diaphragm anterolaterally and move the esophagus into a more anterior and lateral position before closing on each side. The esophageal hiatus should not be so tight that the forefinger cannot be inserted.

greatest causes for postoperative complications; namely, the great increase in intra-abdominal pressure which interferes with respirations, causing anoxemia. Usually in older children there will be enough room in the abdomen and thoracic operation is desirable.

Congenital absence of the posterior portion of the diaphragm usually occurs because the diaphragm simply does not form from the pleuroperitoneal membrane. The defect usually extends from the eighth rib posteriorly and medially to the esophageal hiatus. This type of hernia does not have a sac; however, the loose areolar tissue may simulate one. This type of hernia is really a greatly glorified pleuroperitoneal hiatus type of hernia. It is in this type of hernia that the intestines are apt to herniate to a high level. Sometimes the kidney or the spleen may be found in the thoracic cavity, and on the right side a great portion of the liver may ascend, although this is rare. The chief concern in the repair of large hernias is finding enough fascia or muscle to close the defect. Many ingenious devices have been suggested, and since there is no diaphragm to use, tissue must be borrowed. The posteroperitoneal fascia may be utilized in obtaining a closure by fixation to the thoracic wall; the phrenic nerve may have to be interrupted so that the diaphragm will not pull against the suture line and also so that the relaxed diaphragm will give a little more material with which to work. Sometimes rib resection is necessary so that this portion of the thoracic wall may be pulled in. Also, the transversalis fascia may be used by making an incision through the peritoneum and turning the transversalis fascia back over the defect. Last, a transplant may be made from the fascia lata as an inlay graft.

Congenitally short esophagus with a partial thoracic stomach is really not a hernia, but it is a stomach which lies high because it has never descended below the diaphragm, and this in turn is due to a congenitally short esophagus. This anomaly usually causes symptoms due to stricture. It may be corrected in many different fashions. If the esophagus is not too greatly shortened, the phrenic nerve may be interrupted and the esophagus mobilized from the arch of the aorta down in the hope that the diaphragm will rise sufficiently so that it can be sutured up around the cardiac end of the stomach, making this an abdominal rather than a thoracic stomach. By interruption of the phrenic nerve, the diaphragm can be elevated anywhere from 2 to 5 cm., and then by separation of the attachment of the esophagus from the hiatus and posterior thoracic wall some 5 to 8 cm. more of this organ can be drawn down into the abdomen. The elevation of the diaphragm and the pulling down of the esophagus is not without danger because it is apt to produce a great deal of tension and pull loose. It is perhaps just as well if there is no stricture or symptoms to let it alone. However, where symptoms are present and gastric retention is present, it may be desirable to attempt to correct the defect surgically. In one case we did an esophagogastrostomy in the manner of

this reason we have adopted the procedure of Ladd in the care of large hernias of this type. Here it is our custom to make an abdominal incision and repair the hernia, and if there is a great deal of intra-abdominal tension, the abdomen is closed incompletely; that is, a ventral hernia is established by leaving the peritoneum open and closing the rectus sheath and skin. The abdominal hernia is then repaired in two or three weeks. We believe it is proper to treat the congenital types of hernia, in infants, regardless of whether they are dome or pleuroperitoneal, by the abdominal approach, particularly if a large protrusion of the viscera is present in the thorax, for the reason that having to reduce them, the abdominal pressure may be so great that closure of the abdomen may be very risky. We have observed that this is one of the

Fig. 246.—Pleuroperitoneal hiatus hernia with partial obstruction. F. L. was a boy 8 weeks old who was brought to the hospital because of persistent vomiting. The x-ray photograph shows a diaphragmatic hernia with most of the alimentary tract in the left pleural cavity. There was great delay in the emptying time of the stomach and duodenum. At operation a large pleuroperitoneal hiatus hernia was found. The pyloric end of the stomach, duodenum, a small segment of jejunum, and the sigmoid flexure were all that remained in the abdomen. There was no hernial sac. A catheter was introduced through the opening in the diaphragm to relieve negative pressure and facilitate reduction. After reduction the defect was closed with interrupted silk sutures. In younger infants the abdominal incision would have been difficult to close. During the eight weeks of life, sufficient growth had taken place to permit primary layer closure of the incision. There were no postoperative complications. (Case referred by Dr. H. Stadler.)

diaphragm really does not belong in this discussion since it is not a true hernia. However, since it may give rise to respiratory symptoms due to embarrassment of respiration, operative intervention may be necessary, particularly in the extreme variety. We have only had two of these cases. In both instances they were corrected by a transthoracic approach and the high diaphragm was simply plicated by fine silk sutures. This procedure worked very well and we believe it is probably the best solution to the problem. However, it was found that in neither of our cases did the diaphragm resume its function, but the thoracic space was greatly increased, thereby relieving respiratory embarrassment. In children the respiratory reserve is not as great as in adults and therefore pulmonary symptoms and signs are more pronounced than the gastrointestinal complaints. These are dyspnea, palpitations, thoracic pain, attacks of cyanosis, sense of suffocation in older children, cough, asthmatic attacks, and, also in the older group, referred pain into the left or right shoulder. Sometimes there are gastrointestinal symptoms, and if the child is old enough, he will complain of pain in the upper abdomen, distention, and vomiting in some cases but not in all. The milder types may produce, as we have seen, very few complaints. On physical examination nothing abnormal is seen or palpated. However, bowel sounds may be heard if there are hollow viscera in the chest. A chest film may reveal the diagnosis. A barium enema and an x-ray examination usually give more information and if no obstruction exists in older children, a barium meal may be given. In the presence of obstruction in the newborn or the very young baby, one must consider a congenital diaphragmatic defect. Sometimes the signs and symptoms of esophageal atresia may resemble those of dome hernia. Therefore, in the newborn, when there is great distention and regurgitation with strangling and cyanosis, one must think of the two types of anomalies that have been mentioned. The associated anomalies in our cases of congenital diaphragmatic hernia have not been as common as in other types of congenital defects. We have found umbilical hernia and malrotation of the midgut with excessively long mesentery as associated defects in three of our cases. Dextrocardia is reported in two of our cases, but we believe that this was due to the collapse of the left lung from pressure in the left chest and mediastinal shift rather than to dextrocardia.

Summary

The only treatment that is curative is the surgical closure of the opening in the diaphragm. The approach should be through the abdomen in the newborn, and the muscle-splitting incision aids greatly in the closure of the incision and the prevention of the postoperative hernia. In older children and adults, the thoracic approach is best. A few practical points in the technique may be emphasized. (1) The child must be free from infections of the respiratory tract. (2) Intratracheal ether anesthesia is best. (3) Abdominal approach through muscle-splitting

a Finney pyloroplasty, and we left the stomach in the thorax, suturing the diaphragm around it after greatly enlarging the hiatus, very much like we do following esophagectomy. This man is perfectly well at this time, some years after the operation. The indications for surgery were partial obstruction of the esophagus with stricture and extreme dysphagia. In fact, there was a beginning megaesophagus formation.

Eventration or very high diaphragm. In this case the diaphragm is immobilized and fixed at a high point. This may interfere with respiration and may give rise to paradoxical respiration. Eventration of the

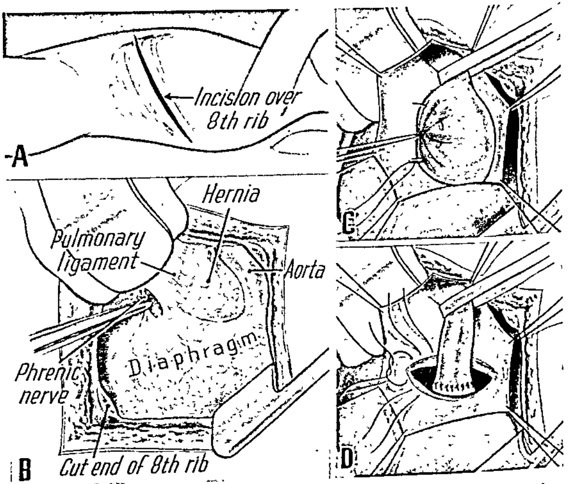

Fig. 247.—Diagrams illustrating transthoracic approach for the repair of esophageal hiatus hernia.

A. The usual incision over the eighth rib or in thin individuals in the eighth interspace without the resection of the rib. *B.* The hernia and contiguous structures. The lung has been retracted upward. The pulmonary ligament is divided and then the phrenic nerve is crushed temporarily paralyzing the diaphragm. The esophagus is freed and the vagi are carefully preserved. The sac is easily identified after incision of the mediastinal pleura. The sac is opened so that the cardiac end of the stomach and esophagus may be inspected for possible ulceration. The posterior wall of the sac is intimately attached to the anterior wall of the stomach so that the sac cannot be dissected free. In this way it resembles a sliding hernia which is described in Chapter 19. The redundant portion of the sac may be trimmed away and then closed and enfolded with a series of purse-string sutures or with interrupted inversion sutures of silk. *C.* Shows the method of purse-string sutures used to enfold the sac. The hiatus is then closed around the esophagus in a manner shown in *D.* Then the pulmonary ligament and mediastinal pleura are sutured with fine silk. It is desirable to make the hiatus large enough barely to admit the forefinger. A tube within the esophagus will guide the surgeon as to the snugness of the hiatus opening.

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The time for the operation should be as soon as the anomaly has been discovered. In our experience, the newborn stands surgery very well if properly fortified with blood and if the fluid balance is controlled. Very often we think that we must improve the condition of these babies. This is not possible in the presence of a large hernia because oftentimes the child actually develops a complete obstruction from an incarceration during the waiting period. Babies are placed in the oxygen chamber and this has been a great help. Should we encounter the congenital types of hernia in the older child, we have invariably used the thoracic approach with great satisfaction.

TRAUMATIC HERNIA

Traumatic hernia really is a misnomer because it is not a true hernia according to our definition. We have defined hernia as "a protrusion of a viscus with a portion of the enveloping membrane through a normal or abnormal opening." It is true that in certain types of congenital hernia, there is a very primitive type of coverning for the hernial protrusion. However, in traumatic hernia there is nothing at all. In other words, this is simply an evisceration or a dehiscence of a suture line in which the abdominal viscera protrude into the thoracic cavity. This type of hernia is easy to diagnose because of the symptoms and signs and x-ray findings. Usually, however, it is thought to be an injury to thoracic organs, and sometimes open thoracotomy is necessary in order to make the diagnosis because there may be both lung and diaphragmatic injury. The diaphragmatic hernia which is the result of an inflammatory necrosis of the muscle caused by subphrenic abscess, or pressure from rubber tubes used in draining empyema cavities, is also a traumatic form of hernia but is very rare. We have seen two of these, one due to the pressure of a tube

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hind gut. The anterior ectodermal cavity or stomodeum is separated from the pharyngeal cavity by the pharyngeal membrane. Portions of this membrane may persist at birth, but this anomaly is rare.

THE FACE, LIPS, AND PALATE

It is through the branchial clefts and arches (primitive gills) that the face, lips, palate, jaws, and neck develop (see Chapter 19). The complexity of this development may be understood by carefully studying the formation of the following chief processes:

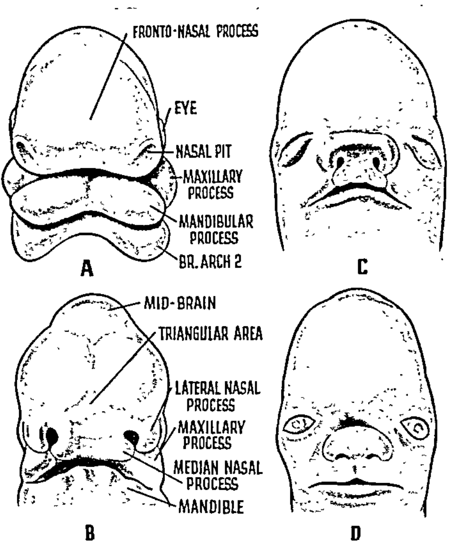

Fig. 248.—Diagram illustrating the development of the human face. (Adapted after Peter, from Arey L. B.: Developmental Anatomy, Philadelphia, 1942, W. B. Saunders Co.) *A*. At 6 mm. (×14). *B*. At 10 mm. (×11). *C*. At 15 mm. (×10). *D*. At 20 mm. (×7.5).

A median nasal process (which appears in the sixth week) in the center of the primitive head above the primitive mouth (which appears in the fourth week).

The medial and lateral nasal processes.

Chapter 20

THE ALIMENTARY SYSTEM

The alimentary tract extends from the mouth to the anus. Before food can be absorbed and used in nutrition, it must be acted upon chemically and mechanically. This action begins in the mouth and is carried on as far as the large intestine, where absorption of water and formation of vitamin K_2 takes place. The refuse is then eliminated through the rectum and anus. The alimentary canal is about thirty feet long.

This chapter will include discussions of the lips, mouth, pharynx, esophagus, stomach, small and large intestines, rectum, and anus. In addition, special organs found within the canal, such as teeth, gums, palate, tongue, and palatine tonsils, must be considered. The accessory glands placed external to the wall of the canal are considered in Chapter 22.

Since the face forms the outer covering of the oral cavity, it is intimately associated with its function and with many of its diseases. Therefore, it, too, should be described. In addition, it is necessary to consider the cavity which contains the gastrointestinal tract (the abdominal cavity) and its lining (the peritoneum), for they are intimately associated with the alimentary system in health and disease.

A description of the development of the alimentary tract is important in order to understand congenital anomalies as well as physiological functions. "An animal in its ontogeny recapitulates its philogeny." Indeed, in the successive stages of development of the human embryo we may trace the development of man from the pisces (fish), through the amphibia (frogs) and the reptilia (reptiles) and aves (birds), especially in the gastrointestinal tract, to the mammalia (mammals).

In the lower animals the digestive apparatus is a simple tube which passes through the center of the body from an anterior or mouth aperture to a posterior or anal aperture. In man this same arrangement exists, but there are certain modifications: (1) The tube is very long (seven to eight times the length of the trunk). (2) Certain portions of the tube have become modified to perform special functions. The mouth has teeth and tongue for mastication and deglutition. The stomach contains gastric glands, producing gastric juice; the small intestine has villi to facilitate absorption. (3) Certain special accumulations of glandular tissue outside the canal (salivary glands, liver, pancreas) are connected with it by ducts and pour secretions into it. These organs have been developed from the tube as outgrowths. They are considered under the glandular system. (4) Even the rectum is a late development in the phylogenetic scale and permits temporary storage of excreta.

In the early embryo the spherical vitelline sac has two entodermal tubes which develop cranially and caudally; these are the fore-gut and hind-gut, respectively. The region between these tubes opens anteriorly into the yolk sac and is known as the mid-gut. At each end the entoderm comes into contact with ectoderm ventrally, forming the pharyngeal membrane of the foregut, and dorsally, the cloacal membrane of the

hind gut. The anterior ectodermal cavity or stomodeum is separated from the pharyngeal cavity by the pharyngeal membrane. Portions of this membrane may persist at birth, but this anomaly is rare.

THE FACE, LIPS, AND PALATE

It is through the branchial clefts and arches (primitive gills) that the face, lips, palate, jaws, and neck develop (see Chapter 19). The complexity of this development may be understood by carefully studying the formation of the following chief processes:

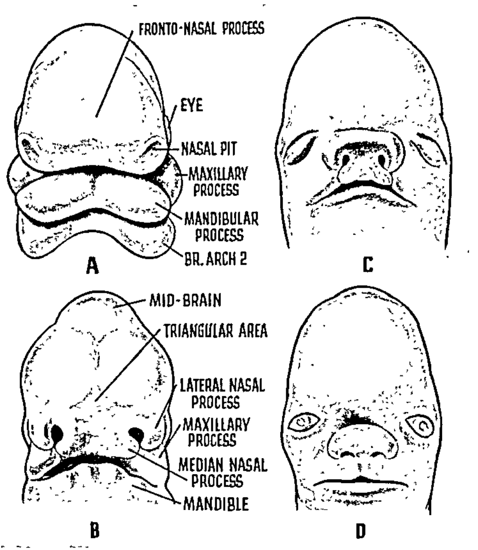

Fig. 248.—Diagram illustrating the development of the human face. (Adapted after Peter, from Arey L. B.: Developmental Anatomy, Philadelphia, 1942, W. B. Saunders Co.) *A*. At 6 mm. (×14). *B*. At 10 mm. (×11). *C*. At 15 mm. (×10). *D*. At 20 mm. (×7.5).

A median nasal process (which appears in the sixth week) in the center of the primitive head above the primitive mouth (which appears in the fourth week).

The medial and lateral nasal processes.

The maxillary processes, which will move toward the center and join the lateral nasal processes.

The mandible, which moves toward the center and fuses.

It is easily seen why most deformities are in the upper lip and palate. This is due to a failure of fusion between the medial and lateral nasal processes in the former case (harelip) and the maxillary processes in the latter (cleft palate), although other anomalies such as leontiasis ossea may result from irregular fusions.

The face is made up of skin and the muscles of expression and is lined by mucous membrane (the mouth). There is no deep fascia, so that the line of the face occurs due to muscular movements. These muscles are the continuation really of the platysma muscle (panniculus carnosus) in the neck, a well-developed structure in lower animals. There are great variations in the development of the various muscles of the face. The orbicularis oris muscle is of great interest in repairs of the upper or lower lip for congenital malformations and after the excision of new growth. This muscle is well developed at the corner of the mouth but quickly thins out as the alae of the nose are reached.

The nerve supply of the face is sensory and motor. The former function is carried chiefly by the fifth (trigeminal) nerve which has three divisions: the ophthalmic, supplying the area about the eyes; the maxillary, supplying the cheeks; and mandibular, supplying the lower jaw area. The chief motor nerve is the facial (seventh cranial nerve), which emerges from the skull through the stylomastoid foramen, just below and posterior to the ear, and is then distributed like a fan over the entire face. The surgeon is careful to avoid the facial nerve by making incisions parallel with it. The tongue is supplied by the hypoglossal nerve.

The arteries of the face come from below upward and are all branches of the external carotid. This is important because facial hemorrhage may be controlled by pressing this vessel against the carotid tubercle (anterior tubercle of the transverse process of the sixth cervical vertebra). The arteries are the external maxillary and the transverse facial; the latter is a branch of the superficial temporal. The chief vein is the facial, which empties into the internal jugular. The angular vein communicates, through the superior ophthalmic, with the cavernous sinus. The lymph flow is from above downward, except about the eyelids, from which the lymph drains laterally into the parotid nodes.

Congenital Malformations of the Lips and Palate

Harelip gets its name from the supposed resemblance to the rabbit lip. It may be single or double. The treatment is surgical repair and is done in the early weeks of life to prevent secondary facial deformities, speech defects, etc.

Cleft palate is a failure of the hard palate (palatine process of maxillary bone) to fuse. Fusion normally proceeds from before backward and therefore clefts may be partial or complete. The treatment is also surgical but is done at about 3 or 4 years of age because it is a much more serious operation and moreover the cleft later becomes narrower. The operation consists in trimming the edges and then suturing them carefully together. In cleft palate this is preceded by lateral incisions and elevation of the flaps. This is done to relieve tension and improve the blood supply.

Wound healing must be thoroughly understood by the surgeon who repairs harelip and cleft palate. Since the closure is made in a contaminated field, surgical trauma must be held to a minimum because it will predispose to infection. Tension on suture lines must be avoided; thus the

lip is mobilized together with the ala of the nose and the palate is pushed back by an anterior curved incision in congenitally short palates. Also in cleft palate repair flaps are elevated and sutured back; then after several weeks or months the flaps are lifted up and sutured. This permits them to form a better blood supply and also allows for more granulation tissue to form on the bed of the shifted flap. In addition, as the flaps are sutured, if tension is still present, only the anterior portion is sewed. Then after two or three weeks the posterior portion is closed. When a child is under anesthesia, the palatine muscles are stretched to get approximation of the palate. On awakening, the shortened muscle which has been drawn abnormally over into the midline becomes active and pulls on the suture

Fig. 249.—Double harelip. In the embryo the central portion of the mouth is formed by the nasofrontal process (median and lateral portions on each side), which unites with the maxillary process on each side to form the upper lip, maxilla, and nostrils. If union fails, an opening remains between the mouth and nasal chamber. If this failure occurs between the median and lateral nasal processes, as here shown, the premaxilla remains isolated, with its two central incisors.

line. To avoid this, the hamular process may be divided or the tensor palatine muscle may be severed. Obviously the palatine artery must not be injured or the blood supply to the flaps will be impaired. Last, some form of splint to obtain rest is used after harelip and cleft palate operations—in the former a special wire adhesive device and in the latter a cemented wire splint which is attached to the teeth. A failure will prevent perfect results by subsequent operations because of fibrous tissue replacement and lack of normal mucous membrane or skin (harelip). Thus the rules to secure repair of tissue by first intention must be observed meticulously so that the factors which delay healing will not occur; namely, in-

fection, poor blood supply, large space to fill in, lack of rest, foreign bodies, and poor general condition of the patient.

Prognathism or the protrusion of the lower jaw may require surgical correction for cosmetic as well as physiological reasons since it may interfere seriously with mastication. Varying with the degree and type of anomaly, the following procedures are available:

1. Resection of a portion of the body of the mandible in the retromolar area, either unilaterally or bilaterally through a submandibular approach. The alveolar nerve should be preserved. The bone ends are approximated with silver wire and the jaw is immobilized by interdental wiring for eight weeks.

2. Diagonal osteotomy and partial resection of the ramus or horizontal division of the ramus. In the latter method the incision is made behind and below the lobe of the ear and parallel with the ramus. The parotid gland is dissected forward. Sectioning should not be lower than one-half inch below the mandibular notch to avoid injury to the inferior alveolar nerve and vessels.

Infections of the Face

Infections of the face may be of the localized type, such as carbuncle, furuncle, and impetigo contagiosa, or of the spreading variety, such as erysipelas, or of the mixed type which in debilitated children starts in the mouth and may give rise to gangrenous stomatitis (noma, or cancrum oris). These and the rarer infections such as tuberculosis, syphilis, actinomycosis, and anthrax have been discussed in previous chapters. It is well to point out that many diseases behave differently on the face than elsewhere in the body. Examples are erysipelas, carbuncle, and lupus erythematosus. This is due to the anatomical and immunological peculiarities of the face as described in Chapter 5.

The lips may be inflamed due to actinic rays (actinic cheilitis), cosmetics (cheilitis venenata), virus (herpetic cheilitis), drugs, and avitaminosis (cheilosis).

Maxillofacial Injuries

Maxillofacial injuries are treated in the same way as injuries elsewhere on the body (see Chapters 5 and 16). However certain special problems peculiar to the face and mouth should be mentioned.

Because of the edema which usually results, an airway must be provided at once, either by nasal tube or tracheotomy.

Blast or tattoo injuries to the face require careful scrubbing with a stiff brush or curette to get out foreign bodies.

Injuries to the eyelids may cause great swelling, thereby obscuring severe injury to the eyeball which may be so severe as to require enucleation.

The external ear should be carefully sutured with nonabsorbable material and allowed to remain in place for two weeks since cartilage heals slowly.

The lips, tongue, and floor of the mouth should be cleaned and sutured; if injury to the latter is deep and cleansing is late, external drainage may be necessary.

The nose requires careful attention, and if a deformity results, cartilage and skin from the ear may be used as a graft. In fracture of the nasal bones a dental mold may be used after replacement of the fragments. Hematomas in the mucoperiosteum should be evacuated.

The accessory paranasal sinuses may be fractured and they may contain foreign bodies which should be removed even if a Caldwell-Luc operation is necessary.

Mandibular Fractures

Mandibular fractures, whether compound or simple, should be reduced promptly and retained by any of the following methods:

1. Interdental wire, using No. 22 or No. 23 gauge stainless steel wire.
2. Inside arch bar attached by interdental wire loops or by tooth bands; this is an excellent method, but a pressure gingivitis may occur.
3. Rubber ligature fixation is excellent but must be strong enough so that muscular action cannot displace the fragments. Wire loops are applied around the upper and lower teeth. Rubber bands hold the jaws together.
4. Instead of rubber bands, small wire may be used to hold the jaws in opposition.
5. In edentulous persons, alveolar wiring or wiring to a tray or splint may be used.
6. Intraosseous, intraoral, and extraoral wiring are indicated in fracture of the mandible and facial bones where it is impossible to maintain these fragments by other methods.
7. The cemented cast metal cap splint with adjustable screw or turnbuckle is useful in many types of fractures and allows for good oral hygiene.
8. Open types of splints made of acrylic or cast metal, locking in the interproximal spaces by projections from buccal and lingual flanges and hinged in the back, are useful in cases where some of the teeth are decayed or missing.
9. External pin fixation is useful only in very extensive fractures with much loss of bone. There inlay grafts are used.
10. Headcap or skullcap traction is used in 9, and sometimes in the edentulous type, maxilla fractures are reduced and maintained by labial arch bar or wiring of lower to upper jaw or by skullcap attachment and wiring to floating segments.

Zygomatic malar fractures should be reduced by the use of tenaculum forceps for grasping the bone through the skin or by the use of elevators

if a compound fracture is present. Direct wiring or external traction with a skullcap may be used. If there is an *associated fracture of the antrum*, this cavity may be packed with gauze through an antrotomy for additional support.

Injuries to the mastoid require curettement of its cells and packing.

New Growths of the Lips and Face

Benign neoplasms such as lymphangioma and hemangioma frequently cause enlargement of the lips (macrocheilia) and tongue (macroglossia). A more important group of benign growths include leucoplakia, white patches on the lining of the lip or palate due to irritation, uncleanliness, or syphilis; *keratosis senilis, small scalelike areas on the lips and face;* and fissures of the lower lip. These may be precancerous lesions and should be eradicated by surgery or radiotherapy.

Carcinoma of the face has been mentioned in Chapter 16. It is more common than any other skin cancer. Three types are seen: (1) basal cell *carcinoma,* (2) *squamous-cell carcinoma, and* (3) *mixed baso-squamous* carcinoma. Although the cause is unknown, many predisposing causes have been mentioned: contact with coal tar products and undue exposure to actinic rays or radioactive substances. Precancerous dermatoses, hyperkeratosis (senile or arsenical), and xeroderma pigmentosum may degenerate *into carcinoma unless protected from actinic rays;* uncleanliness is a factor. Facial cancer may occur anywhere on the face; however, basal-cell carcinoma is rarely observed below a line connecting the lobe of the ear with the mouth. Basal-cell carcinoma practically never metastasizes, whereas squamous-cell lesions of the face do so *only rarely.* The spread is by direct extension, and regional nodes are involved only in very late or traumatized (by inadequate x-ray or surgical or mechanical means) cases. In this regard squamous-cell cancer of the face differs from the same lesion of the ear or lip.

Diagnosis is made by biopsy since some other lesions resemble carcinoma: keratosis senilis, pigmented basal-cell carcinoma (may resemble malignant melanoma), fungus infection (actinomycosis, blastomycosis), mycosis fungoides, leprosy, leishmaniasis, syphilis, *and* tuberculosis.

Treatment is by radiation therapy, desiccation, or surgery. The former is indicated in very late cases or in those where operation is contraindicated because of the poor condition of the patient or inaccessibility of the growth. It should not be used where *cartilage or bone* is involved. Desiccation is useful in small superficial lesions followed by curettage and then more desiccation until all of the growth has been removed. This may be followed by the use of x-ray. Wide surgical excision is the treatment of choice. *Certain areas* require special care lest recurrence take place. First, the vasolabial fold close to the ala nasi; tumors here are apt to involve the superior maxillary bone and antrum (even bilaterally). *Cancers*

of the maxillary sinus may be primary and may extend to the face. Second, tumors of the nose involving the septum and ethmoid cells, which is almost impossible to extirpate.

Carcinoma of the ear is characterized by ear lymph node metastases and therefore requires extensive local excision, even lobation of the ear followed by preauricular and cervical node excision. Otherwise cancer of the face does not require dissection of the neck.

Recently, the old method of chemical destruction for squamous-cell carcinoma has been advocated. In carcinoma of the nose the area is treated with dichloracetic acid and as soon as it turns white, zinc chloride paste is applied. Biopsies taken from the margin show whether all of the growth has been removed.

Late cancer is treated by wide excision or destruction by electrocoagulation and by x-ray.

In all cases reconstruction should be attempted at the time of excision. Where destruction of the lesion has been effected by electrocoagulation, skin graft and plastic maneuvers may be advantageously delayed.

Carcinoma of the upper lip is very rare in our experience. Mixed tumors of the upper lip do occur as in the parotid gland. In the lower lip cancer spreads by lymphatic embolism to the cervical nodes—rarely beyond. Therefore, even in late cases with extensive local extension, excision of the carcinoma with dissection of the lower lip, mandible, and lymph nodes is indicated. Some authorities state that routine neck dissection is not necessary in early cases where no palpable nodes are found, if the patient is watched closely. Others aver that it should be done routinely. We have "sampled" nodes of the first echelon and if uninvolved we have not done a radical neck dissection.

THE MOUTH, TONGUE, AND JAWS

The epithelium of the mouth (buccal mucous membrane) is lined with mucous (apical) glands which lubricate it. However, the mouth is kept moist by the secretion of the salivary glands, which aids in the digestion of starch (ptyalin).

The teeth are set in the alveolar processes of the maxilla and mandible and are covered by gingiva (gums). The tooth is adermal structure, not bone, and is composed of dentine (mesodermal) which is covered by enamel (ectodermal) on its exposed surface and cementum (mesoderm) on its embedded part. In the center is the tooth cavity, or pulp, which contains a soft substance (pulpa dentis), through which nerves and vessels run. The tooth has a root (buried part), a neck (covered by gum), and a crown (the exposed part). There are twenty milk or deciduous teeth, which appear between the sixth and the twenty-fourth month of life. These fall out and are replaced by thirty-two permanent teeth, which begin to appear at about the seventh years and are complete by the twenty-third year. There are four kinds of teeth: incisors, cuspids, bicuspids (premolars), and molars.

The tongue is a muscular organ which is very rough, due to the papillae. On its pharyngeal surface are lymph follicles (lingual tonsils). Within the muscle of the undersurface of the tongue are the mixed serous and mucous glands—glandulae linguales

anteriores (Blandin or Nuhn). The blood supply is the lingual artery, and the nerve supply, the hypoglossal nerve. Sensation is carried by the glossopharyngeal nerve (which supplies the posterior part and carries afferent impulses by way of the sinus branch to the carotid sinus, see Chapter 14) and the inferior maxillary nerve (which supplies the anterior part), and taste by the glossopharyngeal and the chorda tympani branch of the seventh facial nerve which supplies the anterior two-thirds of the tongue.

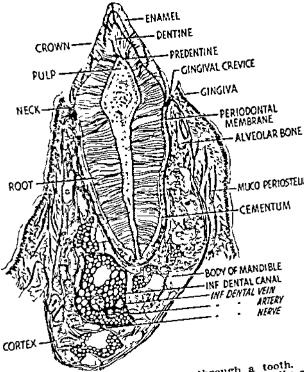

Fig. 250.—Diagram of a longitudinal section through a tooth. The gingival crevice is not normally as wide as indicated. Alveolar abscess is usually associated with caries of the tooth involved. It usually burrows between the periodontal membrane and the alveolar process, and ruptures, or is incised, at the gingival crevice. It may, however, loosen the tooth, invade the mandible or the maxillary antrum, or spread under the gingiva or buccal mucous membrane. Root abscess results from infections which follow down the devitalized pulp and are lodged at the root. These infections are usually not suppurative and do not produce symptoms because the reaction is mild and the area involved, deep. (See Fig. 25.)

Injuries to the Mouth and Tongue

Injuries to the mouth and tongue are usually lacerations which become secondarily infected. A clean incision may heal by first intention. If lacerated wounds are thoroughly cleansed and sutured loosely, they may do likewise. The lower jaw is frequently fractured by a blow or fall. The diagnosis is easy because the teeth do not align properly. X-rays reveal the exact location of the fracture. The treatment consists of proper alignment and then wiring the teeth in the region of the fracture; in addition, fixing the lower to the upper teeth as previously described. The patient must subsist on liquid nourishment. Scrupulous cleanliness in the mouth is advisable because the inevitable presence of bacteria predisposes this region to infection. Absorption of toxin from a mouth infection may lead to septicemia or aspiration pneumonia. Locally, osteomyelitis may and frequently does develop.

The salivary glands are occasionally injured (usually incised wounds). Extreme care in the handling of these tissues, together with rigid asepsis, will make the formation of a salivary fistula unlikely. Occasionally the salivary ducts are cut. These should be probed from within and through the wound and then sutured. Should a salivary fistula result, the law of fistula applies (Chapter 5). If the fistula persists, x-ray treatment over the gland will destroy its function, permitting the fistula to heal. Many occupations produce lesions of the mouth which may be classified as abrasions (holding nails in the mouth), decalcifications (explosive factories, acid dippers); caries (sugar dust); pigmentation (copper, silver, lead on the gingivae); inflammations (cheilitis from actinic rays, cosmetics, phossy jaw from phosphorus poisoning, mercury poisoning); circulatory disturbances (bleeding gums in benzene workers, lack of vitamin C); neoplasm and degeneration (from radium, actinic rays).

Infections of the Mouth (Stomatitis)

Acute catarrhal stomatitis is a nonspecific inflammation of the mucous membrane caused by irritants such as condiments, excessive smoking, and poisonous drugs where there is a low general resistance. The mouth becomes red, swollen, and painful. The treatment is rest, a bland diet, and occasional mouth wash of normal saline solution.

The mucous membranes of the body are supplied with lubricating mechanisms (glands). Their product is protective and antiseptic. It is therefore unwise to use mouthwashes to excess. Even though harmless ones be used, they wash away nature's protective barrier and may actually induce a stomatitis. The same may be said for vaginal douching and rectal irrigations.

Gangrenous stomatitis (noma) has been described previously (see Chapter 6).

Aphthous stomatitis (thrush, or canker sore) may be caused by a fungus, *Oidium albicans* or *Monilia* (*Candida*) *albicans*, and occurs in association with avitaminoses, bacterial infections, and irritations of the mouth, and manifests itself by small yellowish blisters or sores in the mouth, tongue, and lips (perlèche). Although it usually occurs in infants and children, it is also seen in adults, especially in those with pellagra and sprue and stomatitis nervosa. Boric acid mouth wash, or the application of 1 per cent silver nitrate solution to the lesions or 2 per cent aqueous gentian violet solution, shortens this self-limited disease. In resistant cases penicillin is useful.

Vincent's angina is also known as trench mouth. It was formerly thought to be due to the spirillum of Vincent and the fusiform bacillus growing in symbiosis. Although these organisms occur in the mouth normally, they are increased in the presence of the disease. However, it is doubtful if they are the specific cause; the condition is probably the result of a mixed infection. The buccal mucous membrane and gingiva become

ulcerated and are covered with granulation tissue which bleeds freely. The gums recede from the teeth. Zinc peroxide in weak solution as a mouthwash and sulfanilamide internally are excellent remedies. Penicillin is useful locally and intramuscularly. In addition, the excessive granulation tissue and tartar should be gently removed and systemic treatment instituted.

Infections of the Tongue

Infections of the tongue are known as glossitis and may occur (as a result of trauma) in the dangerous acute form or in the less fatal chronic form which may result from hypertrophied papillae and uncleanliness. The tongue may be cleansed by using one of the various digestant powders or liquids. These dissolve the food particles which have accumulated between the papillae.

Leucoplakia may be due to mechanical, chemical, or thermal irritation or to infection as has been described, or it may be carcinomatous. It is a "keratosis" of the mucous membrane which may correspond to a collus or hypertrophy seen in the skin. It may, however, be invasive, in which case it is carcinomatous. A biopsy should be done. If benign, escharotics or cauterization may be necessary after all possible causes have been eliminated. Carcinoma requires excision or radiation.

Simple ulcers occur on the tongue as a result of jagged teeth or improper denture. They are innocuous but should be treated with 5 per cent silver nitrate after their cause has been corrected. The danger is carcinoma. Tuberculosis, syphilis, and actinomycosis also occur in more or less typical form. Glossitis, associated with monilia, occurs in sprue, pellagra, and other avitaminoses.

Infections of the Jaws

Although dental caries is probably not due to an infection (but to hereditary causes, vitamin deficiency, mineral shortage, dietary indiscretions, etc.), it does open the way for infection to invade the dentine, pass into the pulp, and work its way outside the root under the periodontal membrane (the periosteum of the alveolar process). The first gives rise to toothache; the second, to alveolar abscess. The patient suffers severe pain, and the gum, buccal mucous membrane, and cheek become swollen. The abscess may burrow up into the antrum (when the abscess is in the upper jaw) or into the alveolar process, setting up an osteomyelitis of the jaw, which may in turn drain to the outside, causing a sinus (see Chapter 21). The treatment is that of an abscess anywhere: Wait for localization, which is aided by heat and the use of hypertonic salt solution as a mouthwash; avoid injury to the pyogenic membrane; therefore, do not perform an extraction, for this would spread the infection; incise and drain the abscess by cutting through the periodontal membrane close to the tooth. Root abscess follows the same path as the above but is said to be much less severe, due to the fact that it is caused by the less virulent *Streptococcus*

viridans. The evidences of such infection are the so-called granulomas at the root of the tooth. Under the microscope these look like fibrosed granulation tissue and are usually sterile. Formerly it was thought that these "tombstones" of previous infections were "silent and symptomless" foci of infection which caused a multitude of ailments. These teeth were ruthlessly, and sometimes unnecessarily, extracted. In Chapter 5 we have learned the symptoms and signs (local and general) of acute and chronic infections and we have studied the proper methods for their control. From these studies one may conclude that a focus of infection to be entirely silent and symptomless must have been completely controlled by nature (pyogenic membrane, local immunity). Examples may be found in the liver, spleen, and kidneys as infarcts, and as the roots of most teeth. They are probably innocuous. Should there be no evidence of tissue reaction to the presence of microorganisms, a contamination rather than infection is present.

Dirty mouths, full of tartar, food debris, and the ever-present bacteria, sometimes lead to pyorrhea alveolaris. This does not imply that "clean" mouths may not have the disease. As a matter of fact, the cause of this painless gum recession is unknown. The formation of tartar may be related to the precipitates elsewhere, such as kidney stones, salivary calculi, and gallstones and may be due to hereditary causes. Perhaps dogs rarely have it because they keep the tartar off by bone gnawing. Infection under a cover of tartar causes a gingivitis which may be serious. Slow, painstaking cleaning up must be carried out to secure a recovery. Any quick, traumatizing methods may cause a diffuse infection. This clean-up should not be done immediately before an operation. Local and systemic use of penicillin before and after this treatment, especially if extractions are done, may minimize the transient bacteremias which may follow such treatment.

Tumors and Cysts of the Mouth, Tongue, and Jaws

The mouth is one of the most frequent sites of *cancer.* It manifests itself as a chronic ulcer or a raised tumor on the buccal mucous membrane, gingiva, or floor of the mouth. It is more common in men, particularly in smokers and chewers of tobacco. All jagged teeth and sources of irritation should be removed, for here chronic irritations are to be feared. Metastasis is by way of the submental and submaxillary lymph nodes. Early and complete removal of the growth and lymph nodes followed by x-ray gives good results. Usually this is not feasible because of the advanced stage and therefore radium is preferable in many cases. However, every effort should be made to remove even advanced growths surgically because of their tendency to remain in the locale in which they start. Intraoral carcinoma may be multiple due to its lateral spread. Occasionally it is multicentric in origin. Rarely adenocarcinoma may arise in the parotid (Stensen's) or the submaxillary (Wharton's) gland ducts.

Benign mucous cysts occur in the apical glands of the mouth and mucous glands of the tongue and should be excised.

The *tongue* is also a frequent site of *carcinoma*, especially on its lateral and anterior edges. Carcinoma is frequently associated with syphilis of the tongue. Any chronic ulcer, fissure, tumor, or chronic leucoplakic area warrants removal by the cautery for microscopic study. Symptoms are pain and interference with speech. Later, a large infected ulcer forms, with excruciating pain, involvement of the cervical lymph nodes, and death from cachexia. The disease may be prevented in a few instances by avoiding chronic irritations by proper dental care. Cure can be produced by removal of the growth, with a wide margin, and the cervical nodes. Radium needles, implanted, give good results. Speech is impaired, but not badly, after resection of half or more of the tongue.

Fig 251.—Carcinoma (squamous-cell) of the tongue.

Tumors and cysts of the jaws are closely related to the teeth. Epulis is any tumor of the gingiva but is usually a fibrous type of benign, giant-cell tumor. Odontomas correspond to teratomas. A composite odontoma is composed of enamel (ectoderm) and dentine (mesoderm); a radicular odontoma is composed of root elements only. The tumor is made up of pieces of malformed teeth in a fibrous capsule. Root cysts, or dental cysts, are small epithelial-lined cavities containing a yellow fluid. They correspond to epidermal cysts in the skin. Dentigerous (follicular) cysts contain bits of teeth in a fibrous wall and are analogous to dermoid cysts. Inflammatory cysts are not uncommon. Their mode of formation has been discussed in Chapters 4 and 15. They are lined with connective tissue which is thick and must be excised if repair is to follow by healthy granulation tissue. Epithelial-lined cysts require complete extirpation. If small bits of epithelium remain, the cysts may recur. Other benign mandibular tumors which may be single or multiple are benign giant-cell, osteitis fibrosa cystica (hyperparathyroidism), fibroma, ossifying fibroma,

fibrous osteoma, fibrous displasia of bone, and cementoma (which is due to reaction of the periodontal membrane). Malignant growths include fibrosarcoma, osteogenic sarcoma, metastatic carcinoma (breast and thyroid), and ameloblastoma (adamantinoma). The latter arise from the dental follicle or the gum. They are epithelial and may result in adamantine carcinoma. Diagnosis of mandibular tumors is by x-ray and biopsy because there is great variation in x-ray pictures of these growths and there is no characteristic finding. Tumors of the upper jaw correspond to those of the mandible. This includes practically all of the tumors that involve bony tissue and, in addition, many cystic and calcified tumors of the odontoma group. Last, tumors of the accessory nasal sinuses, the nose, and oral cavity may invade the superior maxilla.

Fig. 252.—Epulis. This was not a giant-cell tumor. There was hyperplasia of the gingival epithelium on a fibrous base, with chronic inflammation. Excision was curative.

The *neck* has not been discussed as an anatomical entity but rather its various structures have been included in their proper place. Fascial planes and infections of the neck are discussed in Chapter 19. Since about 85 per cent of the cases of Ludwig's angina follow the extraction of the lower molars or the posterior bicuspids, it is well to mention here that the extraction of teeth may have serious potentialities.

Lymph nodes in the neck are discussed in Chapter 17. Very often a posterior pharyngeal or intraoral carcinoma is overlooked and the first evidence of the growth is in the cervical nodes. Not too rarely cervical node metastases are the first evidence of carcinoma of the thyroid and salivary glands and of structures below the clavicle (breast, lung, esophagus, pancreas, kidney, and adrenal).

Neoplasms in the neck which are primary may be related to the salivary glands, thymus, thyroid, and parathyroid glands (Chapter 22). Some of the rarer neoplasms should be mentioned: primary carcinoma of the eustachian tube; primary growths of the salivary gland (papillary cystadenoma lymphomatosum, pseudoadenomatous epithelioma which is benign, Hashimoto's massive lymphocytic salivary adenitis); branchial

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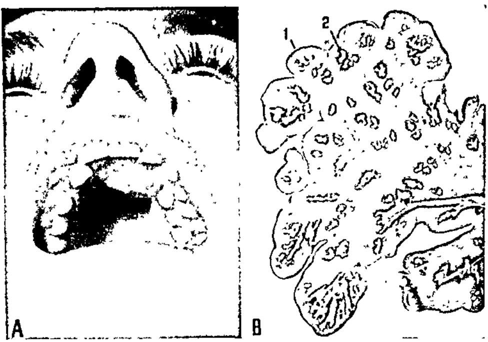


Fig. 254.—Squamous papilloma of mucosa *A*. Clinical photograph showing tumor of mucous membrane covering gingiva. *B*. Summar photograph showing (*1*) epithelium and (*2*) vascular core of papillus.

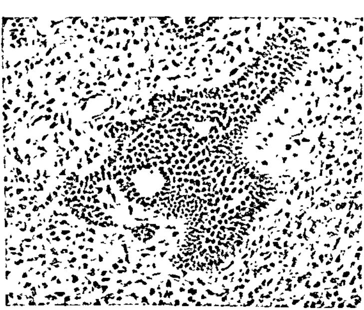


Fig. 255.—Adamantinoma The columnar cells around the periphery are the enameloblasts. The center is filled with these cells which have degenerated.

cleft tumors (pseudoadenomatous epithelioma, benign, branchiogenic carcinoma); thymus (*malignant thymoma, hygroma*); thyroid and parathyroid (Riedel's struma, Hashimoto's disease, aberrant thyroid, Hürthle-cell carcinoma, adenoma of the parathyroid, *adenocarcinoma of parathyroid*, liposarcoma); and tumor of the carotid body, ganglioneuroma, Schwannoma (Chapter 18) liposarcoma, and rhabdomyosarcoma. The *diagnosis in some cases is made by the presence of the growth and biopsy*; in others, by secondary effects such as osteitis fibrosa cystica from parathyroid *adenoma or carotid sinus syndrome from a tumor of the carotid* body. Excision of the growth in every instance is the treatment of choice wherever feasible.

Fig. 253.—Dentigerous cyst. The undeveloped tooth is surrounded by a fibrous sac.

Sarcoma of the jaw occurs either as osteogenic or fibrosarcoma. *Carcinoma of* the jaw is secondary to carcinoma of the mouth or antrum. The treatment of the benign tumors and cysts is local excision, including removal of the epithelial lining about the cysts. The malignant types *may* be *treated* by radium implantation rather than radical resection. However, the latter are preferable *if feasible, including* hemiresection of the mandible. Jaw function may be restored by proper appliances and bone and *soft* tissue grafts.

The veins form a plexus on the exterior of the esophagus from which branches pass in the lower part to the coronary vein of the stomach and higher up to the azygos and thyroid veins. The plexus in the lower part of the esophagus, as in the rectum, forms a free communication between the portal and systemic venous systems. In obstructions of the portal or coronary veins, esophageal varices may form and may bleed profusely (see Chapter 18). The same is true of the hemorrhoidal plexus in the rectum when obstructions to the inferior mesenteric or portal vein are present.

The lymph vessels pass to the deep cervical nodes in the neck, the posterior mediastinal in the thorax.

The nerve supply is derived from the recurrent laryngeal and cervical sympathetic in the neck and the vagus and sympathetic in the thorax.

The act of swallowing is divided into three stages. The first is under voluntary control and is brought about by the action of the tongue and lingual muscles. A pressure of 20 cm. of water is developed in the posterior part of the mouth (a negative pressure is normal in the anterior part of the mouth and in the closed mouth). The second stage is brief and consists of involuntary or reflex contraction of constrictor muscles (see first part of chapter). A negative pressure amounting to 35 cm. of water is created in the pharynx and esophagus, thus aiding the descent of the bolus. In the early days of esophagectomy, when the upper end of the esophagus was exteriorized for further extrathoracic anastamosis, the force of the swallowing reflex was easily demonstrated. In an adult, liquids could be forced for twelve to fourteen inches outside the neck.

The third stage is also involuntary. Food is carried by peristalsis to the cardiac sphincter which is closed except when the peristaltic wave approaches.

The embryology of the fore-gut has been described in Chapter 19. Congenital anomalies have also been mentioned. They consist of atresias, duplications, and enlargements.

Congenital Atresias

We have, in the 2 mm. stage embryo, an entodermal tube, blind at both ends, known as the head and tail folds, respectively. In the former there is a membrane that separates the fore-gut from the stomodeum which goes to form the mouth. This is known as the pharyngeal membrane. The same thing is true in the hind-gut where the blind end is separated from the proctodeum. The latter is known as the anal membrane. Therefore, in the 2 mm. embryo this pharyngeal membrane separates the ventral ectodermal cavity or stomodeum from the pharyngeal cavity of the fore-gut. However, by the 3 mm. stage the membrane is perforated and the stomodeum and the fore-gut becomes a continuous channel. The fore-gut extends from the oral cavity, then to the duodenal papilla, and gives rise to or is differentiated into the pharynx, trachea, lungs, esophagus and stomach, first portion of the duodenum, and the pancreas and liver. The gut is suspended from the dorsal body wall by the dorsal mesentery. In the diagram we have indicated the development of the respiratory organs as well as the esophagus. It will be noted that at first in the 2½ mm. embryo, the respiratory anlage is simply a pouch which has been formed by a groove in the floor of the entodermal tube, just caudal to the pharyngeal pouch. This groove produces an external ridge on the anterior wall of the tube, a ridge which becomes larger and rounded at its caudal end and which is known as the lung bud. The laryngeal or the laryngotracheal groove, as it is called, and the ridge are the forerunners of the larynx and the trachea. The rounded end which we mentioned is the unpaired forerunner of the lung. Externally two lateral longitudinal grooves form, which are the dividing line between the esophagus posteriorly and the trachea anteriorly. By the time that the embryo has reached the 5 mm. stage, the lung bud has divided. These lateral grooves become deeper, and finally a septum is formed which grows superiorly, separating first the lung anlages and then the tracheal tube from the esophagus. The trachea is not developed from the branchial pouches but may correspond with the air bladder of

THE ESOPHAGUS

The esophagus is the part of the alimentary canal which connects the pharynx with the cardiac end of the stomach, passing through the esophageal hiatus in the diaphragm. It lies behind the trachea and the left bronchus. At about the level of the cricoid cartilage pharyngeal and esophageal muscles merge (cricopharyngeus muscle) and form a constrictor mechanism. Just above this point, on the posterior side, esophageal diverticula form (of the pulsion type), if the constrictor does not relax properly in the act of deglutition. Another sphincteric mechanism is present at the cardiac end of the stomach, although a definite cardiac sphincter is not demonstrable.

The gullet extends from the inferior border of the cricoid cartilage and opposite the sixth cervical vertebra to the cardiac orifice of the stomach opposite the eleventh thoracic vertebra, below the diaphragm. It is in the median plane except high in the neck where it lies slightly to the left and continues in this line of the arch of the aorta at the level of the fourth thoracic. Lower down, posterior to the pericardium, it again passes to the left and at the same time forward in order to reach the esophageal opening in the diaphragm which is placed anterior to and to the left of the aortic opening, maintaining this direction until the stomach is reached. In addition to its lateral deviations, it is curved anteroposteriorly to follow the curves in the vertebral column in its upper two-thirds. The esophagus is about ten inches (25 cm.) long and varies from one-half inch (13 mm.) to one inch or more (25 mm.) in the fully distended state. There are three constrictions reducing the lumen to about 23 mm., one at its beginning, another where it is crossed by the left bronchus, and a third where it passes through the diaphragm.

The length of the esophagus varies from 8 to 14 inches (20 to 35 cm.). The distance from the upper incisors to the beginning of the gullet averages about 6 inches (15 cm.). In its course the important relations are as follows: (1) In the neck, anteriorly the trachea to which the esophagus is loosely attached, laterally in the groove between the pharynx and trachea lies the recurrent laryngeal nerves (see Chapter 22), the carotid sheath and its vessels, the corresponding lobe of the thyroid gland, and the inferior thyroid artery. Since the esophagus deviates to the left here, the relations are more intimate on this side. (2) In the thorax, the trachea is anterior to its bifurcation (level of fifth thoracic vertebra); immediately below this it is crossed by the left bronchus, then the pericardium. Posteriorly are the vena azygos, the thoracic duct (which in its upper portion is on the left and may cross it anteriorly and thereby be injured in surgery), the upper five aortic intercostal arteries on the right side, and, in its lower part, the thoracic aorta. The vagus nerves form a plexus which finally forms a left trunk which winds anteriorly, and a right which is posterior. These trunks are severed just above the diaphragm in the operation of supradiaphragmatic vagotomy.

The esophageal wall is composed of the following: (1) Tunica mucularis (longitudinal outer and circular inner layer); the outer layer of longitudinal muscle is covered by adventitia and not serosa. Slips of muscle pervade this layer, attaching the esophagus loosely to the left pleura, left bronchus, pericardium, aorta, and other structures. The absence of a serous coat is important in surgery because of the possibility of leakage. The mediastinal pleura covers the esophagus. (2) Submucous coat which is made of areolar tissue and contains racemose mucous glands. (3) The mucosa which is stratified squamous epithelium thrown into folds.

The blood supply of the esophagus consists of small branches derived from (1) the inferior thyroid artery in the neck, (2) the bronchial arteries and the thoracic aorta in the thorax, and (3) the left gastric and inferior phrenic in the abdomen. The weak area so far as blood supply is concerned is the middle third of the esophagus and therefore anastamoses are usually planned so that the inferior thyroid or gastric-phrenic branches will ensure a good blood supply. However, even the middle third will heal if suture lines are carefully made.

bony fishes. In the 4 mm. embryo the lung bud is present and in 5 mm. embryos the primary bronchus has formed. However, it should be said that before the trachea bifurcates to form the primary bronchus, there appears on the right side the tracheal bud of the upper lobe of the right lung. This bronchial bud is developed only on the right side and appears in the embryos of the 8 and 9 mm. stage. Therefore, we may state that the right bronchus is a direct development of the originally bifurcated lung bud and is really to be considered as a continuation of the trachea, the left side being an offshoot of the former. Within the esophagus the development is of such a nature that the anomalies may occur.

This is due to the fact that the esophagus is originally a vacuolated tube. It really looks like two or more tubes as one sees it from above. In the early embryo it is said to be due to the fact that like the rest of the alimentary canal, the mucosa is laid down first. However, in the esophagus, mucosa is of a stratified squamous type. In its development this becomes ciliated and low columnar, but this changes before birth. The glands of the esophagus are purely mucous. We call attention to this intrinsic development because of the possibilities of obstructions due to persistence of membrane or vacuoles as we have termed them, and in this regard they resemble the same type of stenosis or atresia which may occur in the duodenum or in other portions of the small bowel. Also it is perhaps correct to assume that this peculiar method of development may be the cause of esophageal cysts or duplications which sometimes occur and which are important clinically because they may resemble congenital atresias with various types of tracheal-esophageal fistula.

It is easy to understand from the foregoing review how various types of anomalies may form in the esophagus and trachea. We are interested here only in the former. The anomalies which may be seen, and we are sure this by no means represents all of them, are illustrated in Fig. 256. Types as originally described by Vogt in 1929 are as follows:

Type 1. Complete absence of the esophagus. This is extremely rare and of course is incompatible with life. However, even here attempts may be made to create an artificial opening in the stomach and in the small esophageal bud if there is any which is long enough to bring to the outside.

Type 2. There is a blind end at both the upper and lower segments, but there is no communication with the trachea.

Type 3. Divided into four subgroups:

- 3 (a) The upper segment communicates with the trachea and the lower segment is blind. This is rare.
- 3 (b) The upper segment is blind and the lower segment communicates with the trachea at or about the level of the bifurcation. This is by far the commonest type.
- 3 (c) Both the upper and lower segments have a communication with the trachea. This is rare.
- 3 (d) The esophagus communicates with the trachea but is open throughout its course. Communication is present as a separate tube.

These subdivisions may be *extended, depending* upon the distance between the two ends and the various types of communication. Further-

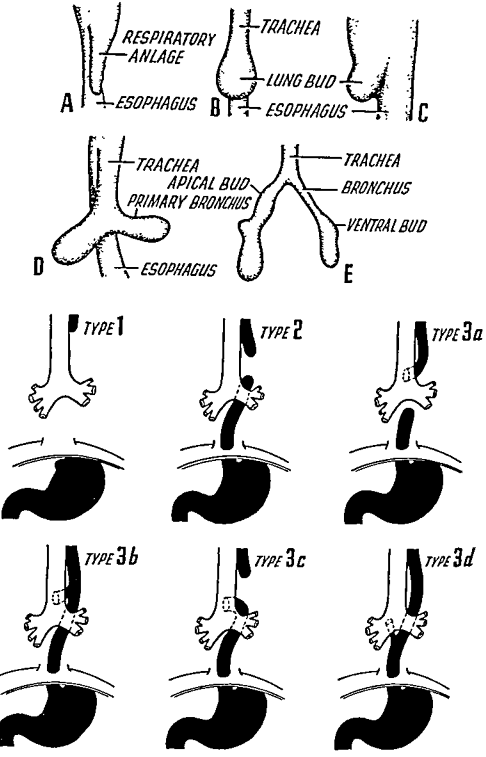


Fig. 256.—Diagrams illustrating the embryology of the development of the esophagus and trachea. (Adapted from Prentiss, C. W.: Laboratory Manual and Textbook of Embryology, Philadelphia, 1915, W. B. Saunders Co.) *A*. At 2½ mm. *B*. At 4 mm. *C*. At 4 mm. in side view. *D* At 5 mm. *E*. At 7 mm. The illustrations below are the various types of congenital anomalies of the esophagus as originally described by Vogt (Vogt, E. C.: Am. J. Roentgenol. 22: 463, 1929). *Type 1*. The esophagus ends blindly and there is no distal end of the esophagus, and the cardiac end of the stomach is also atretic. *Type 2*. The upper and lower ends of the esophagus are present; however, they are both blind, and there is a short distance between them. *Type 3a*. The upper end of the esophagus communicates with the trachea. The lower end of the esophagus is blind. *Type 3b*. The upper and lower ends of the esophagus are in continuity, however, there is a tracheoesophageal fistula. *Type 3c*. The upper end of the esophagus is blind; the lower end communicates with the trachea close to its bifurcation. This is by far the more common variety. *Type 3d*. A variation of *Type 3b* which we have encountered showing the esophagus to be continuous, but there is a tracheoesophageal fistula low down in the esophagus.

catheter will slip down into the stomach, and yet as it is pulled out and the small amount of Lipiodol is injected, some of the oil will find its way into the trachea. Esophagoscopy helps in the diagnosis of this type. Type 3 (c) will give rise to the symptoms of both 3 (a) and 3 (b). Type 2 will show the catheter in the blind upper segment and there will be no gas in the stomach or intestines. In such cases a preliminary gastrostomy is safe and will permit the injection of Lipiodal to determine the distance between upper and lower blind segments so that the subsequent operations may be properly planned.

It may be seen that when the nurse reports difficulty in swallowing, with choking spells, that this anomaly must be considered, and that really a scout film of the thorax and the abdomen immediately gives one the right clue, which may be definitely proved by the methods which have been described.

Treatment requires immediate operation. This consists of a direct anastamosis between the two ends of the esophagus, and this must be preceded by a ligation of the tracheoesophageal fistula if this exists. It is possible to mobilize the esophagus over a distance of approximately 2 to 3 cm. Wider gaps than this are difficult and in such instances the upper end of the esophagus must be brought out through the neck and a gastrostomy must be established; then an external subcutaneous tube must be fashioned or the stomach mobilized and brought up into the neck. This outside tube or stomach mobilization may be made when the child is older. The artificial esophagus may be made by a loop of jejunum transplanted under the skin or of skin entirely. However, reports of the former have not been numerous in American literature, particularly following esophageal anomalies, but they have been reported in connection with strictures and other defects of the esophagus in adults. It is to be desired that a direct connection be established. At best, the artificial subcutaneous esophagus is subject to many complications, and it requires constant attention, although recently Ladd has reported several such cases which have been successfully completed. The classical operation as originally outlined by Richter and first successfully done by Haight is as follows:

An incision is made in the right paravertebral area, extending from the level of the second to the level of the seventh rib. The incision is curved slightly outward, the muscles retracted, and the second, third, fourth and fifth ribs partially resected, subperiosteally. The seventh may be divided, not necessarily resected. Intercostal bundles are tied and the pleura is pushed forward, being careful not to tear it and thereby produce a pneumothorax. Sometimes the azygos vein is in the way, and it must be ligated and divided. The mediastinal pleura is opened and the upper end of the esophagus is easily identified by having the anesthetist or an assistant place a catheter in the blind upper end. The vagus nerve is a good guide. The fistula is doubly ligated with silk and divided, the

more, it may also be subdivided according to whether or not the communication is with the right main stem bronchus or the posterior trachea. The incidence of these anomalies varies with different groups of statistics. After a careful review of the literature it would appear that one may expect to see one of the types of esophageal anomalies in about twenty-five hundred births. This is an equivocal statement and various statistics give it as common as one in three hundred. It is probably true that the former figure is more in accordance with the actual incidence of these anomalies. Of all the types, however, type 3 (b) is by far the more common, accounting for approximately 90 to 95 per cent of all esophageal anomalies. We have observed and treated all types except 3 (a).

Symptoms and signs of the anomaly: Any infant who has more than a minimum amount of mucus should be carefully watched after birth. If, in addition, the child strangles when water or milk is given, one should become suspicious of this anomaly. The most important symptom is this attack of choking and cyanosis, which is aggravated when fluid is given by mouth. There is immediate regurgitation, choking, coughing, cyanosis, and evidence of aspiration of the material. As the infant lies in his crib, mucus drools out of his mouth, and this is excoriating because it contains gastric juice which has found its way into the bronchial and tracheal channel. In addition, there is great distention due to the fact that there is a communication between the trachea or bronchus and the stomach. The diagnosis is easily established without the use of Lipiodol. The following rules should be noted in making the diagnosis:

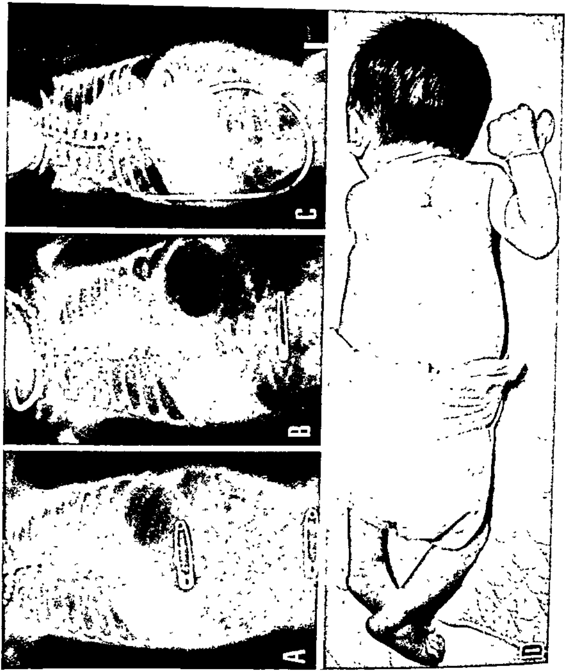
1. When the lesion has been suspected, all nourishment should be stopped by mouth.

2. Barium is absolutely contraindicated and should not be given under any circumstances because it will cause a severe pneumonitis which is apt to be fatal.

3. If it is decided that Lipiodol is necessary, a very small amount is needed; namely, approximately ¼ of 1 c.c. If a large amount is given, it will be aspirated and the child may lose his life by suffocation. Furthermore, Lipiodol is irritating to the bronchial and pulmonary tree. In fact, all that is needed is a No. 8 or 10 rubber catheter which may be inserted to show the blind pouch in the x-ray. This, in addition to enormous distention where no food has been given and where mucus and saliva and irritating juice drools from the mouth, gives clear evidence of a blind upper end and a communication of the lower end with the bronchial tree. Should the anomaly be a type 3 (a), every effort at swallowing will produce violent coughing and cyanosis and there will be no gas whatever in the gastrointestinal canal as detected by x-ray. A catheter may find its way into the trachea, giving rise to a coughing episode. The other types which have been mentioned may give rise to some difficulty in diagnosis. Here again, if type 3 (d) is present, the

Fig. 257.—Congenital atresia of the esophagus, type 3c. *A.* X-ray photograph showing the blind esophagus with an opaque catheter introduced within its lumen. The stomach and intestines are filled with gas, indicating a tracheoesophageal fistula. This is really all the information that is necessary in order to make the diagnosis of type 3c. *B.* However, a small amount of Lipiodol was introduced in the blind esophagus and immediately the child regurgitated this and aspirated it into the trachea. In this way a bronchogram of both lungs was made. *C.* X-ray photograph showing the condition of the patient eight days after surgery. The esophagus is patent, as demonstrated by the catheter introduced from above. The lower catheter is introduced in the stomach through a gastrostomy opening which was made on the day following surgery. *D.* Clinical photograph showing the child after two weeks ready to be released from the hospital.

This infant was operated upon twenty-four hours after birth. A variation of this sequence may be practiced in infants that are not in good condition. The gastrostomy may be done first and continuous suction applied, thereby preventing regurgitation into the lungs. After the child has improved somewhat, then the operation may be done as follows: An incision is made medial to the right scapula, and the fourth rib is resected throughout a distance of about two inches or more. The pleura is carefully stripped and the ribs are spread apart. The azygos vein should be ligated and divided. The upper end of the esophagus is easily identified due to the fact that the anesthetist may introduce a catheter, thereby showing it very clearly. The lower end is easily found by tracing the trachea, downward, and the fistula is encountered usually just above, the bifurcation on the posterior side. The fistula is divided and the proximal end doubly ligated. The distal end is then sutured to the proximal end of the esophagus in an oblique manner, thereby increasing the diameter of the suture line. Two small Penrose drains are introduced in the retropleural space. At no time is the pleural cavity opened. The muscles and skin are then closed with interrupted sutures. This patient was last seen in September, 1949, and is in good condition. He is now 2 years of age and has not required any dilations. (*Case referred by Dr. M. Salzman.*)


A
B
C
D

above factors, fibrosis may occur as a result of ulcer or of chronic esophagitis with resultant strictures. Esophagogastrostomy or partial esophagectomy may be necessary in advanced cases. In early lesions dilations with bougies or pneumatic bag may be done. The treatment of the associated diaphragmatic hernia has been described in Chapter 19.

Duplications of the esophagus are usually blind cystlike cavities which have been described in Chapter 19 and which behave as other mediastinal cysts or tumors. Excision should be done and if a connection exists with the esophagus, this must be closed.

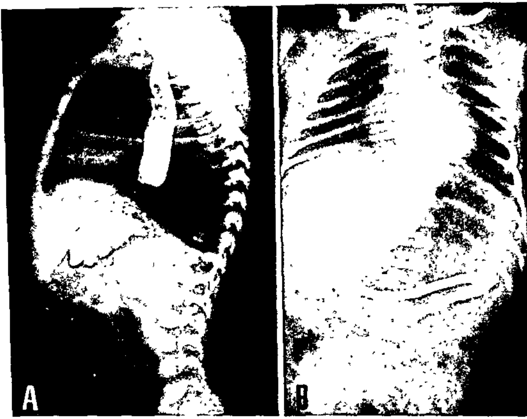


Fig. 258.—This infant was brought to the attention of the surgical department when he was 2 days old because of regurgitation of all fluids. *A*. Barium study showed a stenosis of the esophagus just above the diaphragm. This was dilated and a catheter introduced as shown in *B*. Feedings were administered by this catheter for several days until the baby's condition improved, and then the esophagus was dilated further. This illustrates a very rare type of congenital stenosis of the esophagus due to a small membrane which is amenable to treatment by dilation. The child recovered and has remained well. No further dilations were required after approximately 3 months of age.

Megaesophagus has been reported in infants. It is thought to be due to some form of obstruction near the cardiac end. However, this stenosis cannot always be demonstrated. In this way "congenital megaesophagus" resembles the true Hirschsprung's disease of the colon. Esophagogastrostomy is the treatment, or if the muscles of the cardia are greatly hypertrophied, simple incision down to the mucous membrane is curative as in the Ramstedt operation for pyloric stenosis.

catheter is then introduced into the stomach, and an anastomosis is made between the upper and lower esophageal segments, not by a transverse suture line, but by a diagonal suture line. This is a very important point and is probably responsible for the fact that no stenoses have occurred to date in our cases where this has been done. The entire suture line is made with fine silk. Penicillin is introduced into the operative field, one small Penrose drain is inserted, and the muscles of the back are closed with interrupted silk sutures and the skin is closed with the same material. Postoperatively the child is placed in oxygen for from twenty-four to forty-eight hours. After the second day a gastrostomy is made under local anesthesia for feeding. This, in our opinion, is preferable to intravenous feeding. The entire operation is done under ½ of 1 per cent Novocain anesthesia. Oxygen is administered during the procedure. On about the ninth or tenth day, water may be given by mouth, and if no leakage occurs, the Penrose drain may be removed. It is wise to keep the gastrostomy open four to six weeks to be sure that a stenosis does not occur, because if this does occur it may be necessary to grasp a swallowed thread so that further dilatation may be accomplished.

Many modifications have been advocated since the first successful operation by Haight. The most important of these is that only one rib is resected. This is the fourth rib, and a liberal piece is removed subperiosteally from the posterior angle well around toward the posterior axillary line. The pleura is then stripped from the posterior thoracic wall and the ribs are spread apart with a small mastoid self-retaining retractor. This prevents paradoxical respiration which in some of our cases has been the cause of a great amount of anoxemia.

A second modification is the preliminary performance of gastrostomy as originally suggested by Bigger. This is not done to feed the child but is done to keep the stomach empty by suction so that regurgitation will not occur and, more important, so that a desperately sick infant can be put into better shape for surgery.

Congenital Stenosis

Congenital stenoses due to webs or membranes are usually transient or may be "broken" with a soft rubber catheter. We have seen two of these.

Congenitally Short Esophagus

Congenitally short esophagus has been described in Chapter 19 in connection with diaphragmatic hernia. Sometimes an associated stricture is present. Various theories have been advanced to explain this. When the cardia sphincter is released from control, gastric juice regurgitates into the esophagus; this in turn causes irregular spasmodic contraction due to esophagitis; in addition, heterotopia of gastric mucous membrane may be present, increasing the acid in the lower esophagus. As a result of the

masticated food, chicken bones, etc.), or infection (sectioning the vagus does reduce esophageal motility, but in the experimental animal the results are conflicting); spasm of the diaphragmatic crura (phrenospasm); scleroderma and acrosclerosis (scleroderma with Raynaud's disease) which produce fibrosis in various tissues (vascular, skeletal, and gastrointestinal); severe anemia.

This concept would put cardiospasm in the same category of other psychosomatic problems, Raynaud's disease, segmental ileitis or colitis, essential hypertension, and peptic ulcer.

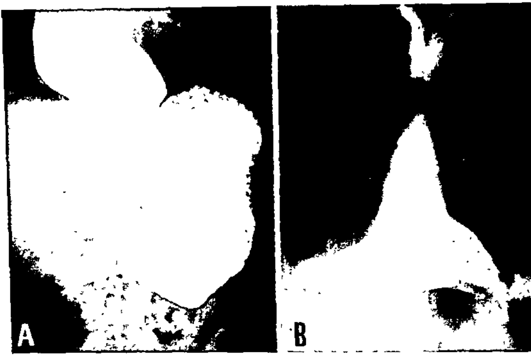


Fig. 259.—Megaesophagus due to cardiospasm and achalasia. *A*, X-ray photograph showing an enormously dilated esophagus which is tortuous. W. N., a man 30 years of age, had complained of dysphagia for many years. Recently he stated that anything he ate, whether liquid or solid, seemed to move no further than the chest and then he was able to regurgitate part of it undigested. In fact, unless he emptied the esophagus, he was unable to move about due to severe chest pain.

The condition is that of cardiospasm or achalasia (meaning without relaxation). The enlargement of the esophagus has been called megaesophagus when it is straight and dolechoesophagus when it is tortuous. The x-ray photograph clearly demonstrates the tortuosity and enlargement of this esophagus Esophagogastrostomy was performed by the transthoracic approach. *B*. X-ray photograph showing the result after surgery. This patient has remained well since operation three years ago. (Case referred by Dr. H. Carpentier.)

Regardless of the cause, whether due to cardiospasm or achalasia at the cardiac end of the esophagus, usually there is little if any thickening, although the wall may be slightly fibrosed in some cases. Above this point there is great dilatation and the esophagus resembles a funnel (megaesophagus) or it becomes dilated and tortuous, resting as a large pouch on the diaphragm (dolichoesophagus). The wall becomes extremely thin and may be pierced by instruments or sharp particles of food. In fact, minute leaks may occur without apparent cause resulting in mediastinitis.

Functional Disturbances of the Esophagus

True reverse peristalsis probably does not exist in the esophagus without obstruction. Reverse wavelets or ripples do occur and are probably responsible for such symptoms as coating on the back of the tongue and regurgitation of fluids. "Heart burn" may be due to the stimulation of the mucosa of the upper part of the esophagus due to regurgitation of acid fluid. Distention by pneumatic bags will produce the symptoms as will the introduction of acid or cold water or excessive smoking. Spasm will also give the burning symptom. In two cases of pernicious anemia with achlorhydria that we saw, heart burn was a prominent symptom. Therefore, acid per se is not the cause and the sensation does not originate in the stomach. Belching is due to reverse waves originating in the cardiac end of the stomach which were thought to relieve the large "magenblasse" or air bubble in the upper end of the stomach after a meal. This is only partially true because some of the air is held in the lower end of the esophagus. Practically all of this gas is swallowed or sucked in. This may be annoying in those who habitually swallow air (aerophagy). Intragastric pressure is not increased as a result of the air swallowing nor is it decreased after belching. Air sucking as opposed to swallowing is seen after operations done under general anesthesia and may be one cause of postoperative abdominal distention.

Cardiospasm is the term used to describe the condition in which the sphincter does not relax properly during deglution, causing dysphagia. Since there is also an incoordination between the muscle of the esophageal wall and the sphincter, the term achalasia has been applied. The cause of cardiospasm is not definitely known. It may be neurogenic in origin and related to a similar condition known as globus esophagitis which has been suggested as a cause. This, in turn, is thought to be due to minute puncture wounds through the esophageal walls, made by sharp particles in ingested food. Ultimately an organic stricture may occur, although fibrosis is not demonstrated. Sometimes it is reflex in nature due to irritation of afferent fibers from the stomach, gall bladder, or other viscera. It may be initiated by intrinsic factors such as irritation of the mucous membrane as previously described. Then, in some, it appears when there is nervous excitation or worry. The sequence in this group may be hurried gulping of food, temporary contraction, and irritation of the mucous membrane which in turn favors spasm. Indeed, an old aphorism concerning the "lump in the chest" which many people complain of after eating while worried avers that "it is not the food, but the mood." "Globus hystericus" represents a nervous contraction of the cricopharyngeus muscle and also produces the "lump in the throat." Other theories as to the cause of cardiospasm are degenerative changes in the cells of Auerbach's plexus at the lower end of the esophagus, possibly due to a vitamin B deficiency; reflex irritability of the vagus nerve which is primary or secondary due to disease or abnormalities in the abdominal viscera, or injury (hard, poorly

observe the esophagus carefully in all positions, including the Trendelenberg. Last, esophagoscopy with a biopsy should be done when indicated.

The treatment includes attention to the general condition of the patient from a neuropsychiatric standpoint and local measures. Attention to the diet (avoidances of rough or hard foods), antispasmodics (atropine), and sedatives (phenobarbital) help. As the disease progresses, dilation with mercury-filled bougies or dilators inserted through the esophagoscope or the pneumatic bag should be tried. If this is not feasible, a gastrostomy is done and retrograde dilations may be started with the fingers and bougies, then followed with the pneumatic bag which is the best and safest of all dilating instruments.

In late cases or in those which do not repond to conservative measures, surgery is necessary. Many procedures have been advocated; namely, (1) extramucous cardiomyomotomy, anterior and posterior. This corresponds to the Ramstedt-Fredet pylorotomy. (2) Cardioplasty with longitudinal incision and transverse suture, like a Heineke-Mikulicz pyloroplasty. (3) Cardiectomy which seems irrational. (4) Phrenotomy (incision in the diaphragm) which creates a hiatus hernia but does not help. (5) Vagectomy and sympathectomy which offer only transient relief. (6) Esophagogastrostomy.

The side-tracking operation is best. It may be done through the abdominal or thoracic approach. We have preferred the latter. The fundus of the stomach is sutured to the esophagus and a horseshoe incision is made very much like a Finney pyloroplasty. The stomach is then anastomosed to the esophagus. In extreme cases of dolichoesophagus the lowermost pouch may not be straightened by this procedure. In this event the dependent pouch is anastomosed to the lesser curvature.

Esophageal Varices

Esophageal varices have been discussed in Chapter 19. They usually occur as a result of cirrhosis of the liver, Banti's syndrome, or thrombosis of the portal vein or splenic vein if the coronary enters it distal to the occlusion. Sometimes there is no apparent cause. The symptoms and signs are those of the primary disease with splenomegaly and ascites and hematemesis. Only rarely is there any other symptom. Often the only symptom or sign is hemorrhage. Diagnosis is made by the history, symptoms and signs, and fluoroscopic examination using barium. With the Valsalva experiment the veins empty; with the reverse Valsalva, they fill. Esophagoscopy establishes the diagnosis.

The treatment is designed to eliminate the cause if possible. Usually this is only partly possible. Less blood enters the portal vein after splenectomy (see Chapter 22). Shunts between the splenic and left renal vein and between the portal vein and inferior vena cava (Eck fistula) offer the best chance of cure. The varices may be removed surgically or injected with sclerosing solutions (5 per cent sodium morrhuate) through the esophago-

The vague methods by which the disease evolves and the more or less characteristic changes which it induces has led to a variety of descriptive terms such as cardiospasm, achalasia, phrenospasm, idiopathic dilatation of the esophagus, esophagectasia, hiatal esophagismus, megaesophagus, simple ectasia of the esophagus, preventriculosis, dilatio fusiformis, and dolichoesophagus. Some observers believe that cardiospasm is a different entity than achalasia.

Symptoms and signs: The disease is usually seen in the third and fourth decades. Dysphagia is present, but it varies from time to time and with the progress of the lesion. Early, it occurs spasmodically and is sudden in onset and may be induced by solid food (usually), but also by liquids. However, it is "all or none" so far as difficulty in swallowing goes. Later there is dysphagia at all times and regurgitation of small, then large quantities of food which at first occurs only once a day, but later, after every meal. Finally, only liquids go through and a large amount of undigested and fermented food is regurgitated after every meal. The entire course of the disease is insidious and the appearance of the patient belies the nature of the process.

Plummer-Vinson syndrome is also called hysterical dysphagia. It occurs usually in women with an unstable nervous system and with associated abnormalities; namely, hypochromic anemia, glossitis, and splenomegaly. The obstruction is usually in the upper end of the esophagus. Treatment consists of repeated dilations with sounds and attention to the anemia and nervous instability. Recurrences are common but once the esophagus is open, other symptoms disappear.

Painful swallowing (odynophagia) is not observed unless there is already a large amount of material in the esophagus which then becomes enormously overdistended. Pain in the chest is different from angina pectoris. Esophageal pain is not related to muscular exercise, but to swallowing, especially highly seasoned foods. There is some loss of weight and no hematemesis. Hoarseness, dyspnea, or cough are not observed, although dyspnea from overdistention and cough from overflow secretion at times do occur.

From symptoms alone the nature of the disease may be suspected. The dysphagia in the early phase may be entirely present or entirely absent. At least it varies greatly from time to time. In organic disease it is progressive, with difficulty in swallowing solid food, first, then soft foods, then liquids. The absence of pain, loss of weight, hoarseness, dyspnea, cough, or bleeding tends to rule out organic disease, although a positive diagnosis cannot be made without fluoroscopic and esophagoscopic study.

In esophageal disease, then, the history, complete physical examination (including mouth, nose, throat, pharynx, larynx, pyriform sinuses and neck, serology), fluoroscopic study of the chest, and fluoroscopic study of the esophagus with barium mixtures are necessary to establish a diagnosis. The roentgenologist should be apprised of the possibilities so that he will

peptic ulcer of the esophagus; fourth, the more specific types of infection, including tuberculosis and syphilis, as well as nonspecific types of infection may produce an esophagitis. Since dysphagia is the chief symptom in all types, a careful examination as outlined previously should be made. This is true in all cases of dysphagia.

Inflammations due to mechanical, thermal, or chemical causes clear up quickly when the causative agent is removed unless there has been destruction of the mucous membrane where fibrosis and stricture result. Bismuth subnitrate in 0.5 to 1.0 Gm. doses is helpful. Ethylaminobenzoate (Anesthesin) in 0.1 Gm. doses is helpful in relieving pain. Penicillin intramuscularly and by insufflation is useful.

Tuberculous esophagitis is treated as tuberculosis elsewhere (see Chapter 7) unless stricture occurs. If the stenosis is in the lower part of the esophagus, esophagectomy and esophagogastrostomy may be done should conservative measures fail.

Syphilis is treated by antisyphilitic therapy and the stenosis which may result is dilatable as a rule.

In all forms of severe esophagitis gastrostomy is indicated to put the esophagus at rest.

Peptic ulcer of the esophagus is probably more common than was formerly thought. The disorder which predisposes to ulceration is hernia of the stomach through to esophageal hiatus into the posterior mediastinum. The hernia may be congenital or acquired and may be reducible or irreducible. The latter may be caused by ulceration, fibrosis, and shortening of the esophagus. Other theories as to its cause are mentioned in the discussion of congenitally short esophagus.

The pathological changes include a recurrent acute esophagitis, then chronic esophagitis with recurrent acute ulceration, then chronic ulceration. The ulcer produces stenosis due to the surrounding induration, and above this is intense inflammation. Sometimes there is perforation or bleeding. Finally there is fibrosis with permanent stenosis.

The symptoms of the acute ulcer are epigastric pain relieved by food and alkalis, heartburn, and regurgitation, especially in the recumbent position or on bending forward. The chief symptom of a chronic ulcer is dysphagia. Often ulcers of the stomach or duodenum are present. Diagnosis is made by careful history, symptoms and signs, fluoroscopy, and esophagoscopic examination.

Treatment should be conservative with ulcer diets, sedatives, antispasmodics, and bed rest. If a hiatal hernia is present, it should be repaired. If stenosis exists, jejunostomy may be necessary for feeding until the ulcer has healed. It should not be done for a fibrous stenosis, which may be dilated by bougies, or, if this fails, esophagogastrostomy should be done. When the hernia is repaired, vagotomy should be done and the splanchnics are infiltrated with novocaine or removed and the phrenic is crushed.

scope, or injection of fibroblastic agents such as dicetyl phosphate may be injected around the esophagus. Resection of the lower esophagus and greater portion of the upper part of the stomach or even total gastrectomy with esophagogastrostomy or esophagoenterostomy will stop esophageal bleeding.

Injuries to the Esophagus

Injuries to the esophagus have been discussed in Chapter 19. Spontaneous rupture does occur in the lower end of the esophagus. Esophagitis or ulcer may be present sometimes. No predisposing cause is found except a bout of drinking, then severe vomiting. The vomiting precedes the pain. In all stomach ailments which may resemble esophageal perforation, the reverse is true. If small, the perforation may heal spontaneously. If large, it must be sutured. (See Chapter 19.) Injuries by strong acids or alkalies are all too common, especially in children, and, when not fatal, leave large raw areas which heal by dense cicatrization. The result is a stricture of the esophagus. These may be treated by repeated dilatations with bougies or dilators and sometimes cured. More often the stricture does not respond and gastrostomy is necessary for feeding. If the stricture is limited to the lower end of the esophagus, esophagogastrostomy will cure the patient. This is not usually the case; the stricture involves a large area and for this reason treatment by any method other than extirpation is useless. Yudin reported eighty cases treated by the "Roux-Herzen" type of esophagoplasty consisting of the construction of a subcutaneous esophagus made from a loop of jejunum. This is done in three stages: gastrostomy, exteriorization of the loop of intestine onto the neck, and its direct anastomosis with the cervical portion of the esophagus. The cicatrized esophagus remains in situ. Sweet has recently applied a much simpler and more practical operation; namely, esophagectomy with mobilization of the stomach high in the thorax and esophagogastrostomy. He believes it necessary to sever the esophagus at the cardia so that complete mobilization of the stomach is possible. Esophagectomy is done so that an end-to-side anastomosis may be accomplished.

Foreign bodies which enter the esophagus usually go through into the stomach. Even open safety pins may do this. However, early x-ray and esophagoscopic examination will reveal the foreign body and permit its removal. Meat impaction may be digested with papain or removed. Sometimes esophagoscopic or manual manipulation through a gastrostomy is necessary.

Inflammations of the Esophagus

Esophagitis may follow mechanical, thermal, chemical, or bacterial trauma. In the first group may be included instrumentation and the presence of a Levine or Miller-Abbott tube for long periods; in the second, hot and cold liquids or solids; in the third, the ingestion of acid or alkalis not sufficiently strong to cause ulceration and cicatricial stenosis; in addition, the acid gastric juice may be a factor in the production of

in the pharyngo-esophageal type) or traction (usually in the large sacs where traction began the process which was continued by pulsion). In the neck, the mechanism of production is like an inguinal hernia. There is a weakness or separation between the fibers of the inferior constrictor muscle of the pharynx and those of the cricopharyngeal muscle, and during swallowing the cricopharyngeal muscle is slow to relax, resulting in a strong pulsion force on the weak area of the posterior pharyngeal wall or the esophageal wall and ultimate bulging of the esophageal wall. Some observers state that the cricopharyngeal muscle does not exist as a separate entity from the inferior constrictor and that the weakness is not congenital but acquired since it rarely occurs before 15 years of age. Since the diverticulum is on the posterior wall, it may point to the left or right side of the neck, but usually it is the former because of the lesser resistance at this point due to the distance of the large vessels of the neck.

Fig. 261.—Traction diverticulum of the esophagus visualized by barium meal. These are not uncommon lesions due to local adhesion and tugging during swallowing. They may occur anywhere along the esophagus but are usually encountered near the hilus where many lymph nodes are present. If they give symptoms, they should be removed or imbricated because they increase in size due to the fact that they are converted into a pulsion type as they enlarge. Then there is danger of spontaneous perforation.

Symptoms and signs of pharyngo-esophageal diverticulum: Food enters this pouch and creates a gurgling sound, or the patient may regurgitate food eaten two or even three days previously. Dysphagia is the chief symptom. Diagnosis is made by the fluoroscopic and esophagoscopic examinations, although the latter must be done carefully lest the thin sac be perforated. The treatment consists of surgically excising the sac. This is done through a longitudinal incision in the neck, with the aid of the esophagoscope, which illuminates the concealed sac. The sac may be easily

In severe cases which remain active in spite of all measures, *esophagectomy* may be done. Since the ulcer originally occurred as a result of hiatal hernia, the operation may be questioned because part of the stomach will be mobilized into the chest. To overcome this criticism, Allison and others have suggested jejunal transplants. However, these too may develop ulcers and therefore resection in addition to careful medical management may be used in the extreme cases. Such treatment should not be required except on rare occasions. Some observers believe that a *radical gastric resection* (four-fifths) of the lower portion of the stomach and pylorus is the treatment of choice.

Diverticula of the Esophagus

Diverticula of the esophagus may be present in the neck (pharyngoesophageal) or in the thoracic esophagus (supradiaphragmatic; epiphrenic). These pouches are said to occur as a result of pulsion (usually

Fig. 260.—Pulsion diverticulum of the esophagus, also known as pharyngoesophageal diverticulum. J. W., a man 45 years of age, complained of increasing pain and discomfort following a meal. Recently he had been forced to make pressure on the right side of the neck, and he was able in this way to regurgitate some of the food which he had eaten and which was not digested. *A* and *B*. Photographs show a fairly large pharyngoesophageal diverticulum. This was removed by a one-stage procedure. The incision was made anterior to the sternomastoid muscle on the right side. The inferior *thyroid artery* and vein and middle thyroid vein were divided, and the right lobe of the thyroid gland was turned medially. The esophagus was identified and the diverticulum was illuminated by the introduction of an esophagoscope by an associate. This made identification of the esophagus very simple, and with the esophagoscope in place the diverticulum was removed and then the edges sutured transversely with two tiers of sutures, using a chromic double zero catgut on the inner tier and silk on the outer. The introduction of an esophagoscope prevents *the complication of taking off too much, and* thereby producing a stricture, or, what is equally serious, leaving too long a pedicle, permitting a recurrence of the diverticulum If possible, the suture line should be made in the transverse diameter. The reason for this is to prevent a narrowing of the lumen, and also the second tier of sutures is more easily introduced in the inferior constrictor muscles since the fibers go transversely. (Case referred by Dr. D. Paris.)

herniation of the mucous membrane through the muscle wall. Its wall is made of mucosa, submucosa, and adventitia. The various layers may be greatly thickened. The cause of this latter type is not known, but it is probably due to a combination of factors such as congenital weakness, cardiospasm, local injuries, or ulcerations. The epiphrenic type of pulsion diverticulum may be the beginning of dolichoesophagus.

Symptoms are dysphagia, odynophagia, regurgitation, anorexia, and loss of weight. The symptoms are episodic. Diagnosis is made by the history and barium examination with the fluoroscope.

Treatment is not necessary for those diverticula discovered by x-ray and without symptoms. When there are symptoms, the pouch may enlarge and should be removed. This is accomplished through an incision in the seventh or eighth left interspace. The mediastinal pleura is incised, the diverticulum exposed and removed, and the opening closed. The mediastinal pleura is left partially open or sutured behind the esophagus so that if infection occurs it may drain into the pleural cavity which is drained by a water-sealed intercostal drain.

Stenosis of the Esophagus

Stenosis of the esophagus may be congenital or acquired and may be caused by external, intramural, and intraluminal factors. Among the external causes are: anomalous vessels (dysphagia lusoria, Chapter 18), mediastinal tumors and cysts, hiatus hernia (Chapter 19), aneurysm. Intramural causes include cardiospasm, scleroderma, neoplasms (benign or malignant), whereas intraluminal abnormalities are due to congenital anomalies, trauma (chemical, such as lye, mechanical, thermal), peptic ulcer, foreign body, spontaneous rupture and fibrosis, feeding tube erosion and stenosis, syphilis, tuberculosis, neoplasms (benign or malignant).

The symptoms common to all are dysphagia, odynophagia, and regurgitation. The diagnosis is made by the history, symptoms and signs, fluoroscopic examination with the barium meal, and esophagoscopy.

The treatment depends upon the cause. (1) General treatment is given for syphilis, tuberculosis, peptic ulcer; in addition, attention is given to water balance, acid-base balance, blood volume, and shock in cases of lye burns and other trauma. (2) Local treatment consists of dilations by bougies or bags. Provision for feeding is made by doing a gastrostomy. This also facilitates dilation. The gastrostomy should be of the Stamm variety so that instruments may be easily introduced. Foreign bodies should be removed. (3) Short circuitive procedures—esophagogastrostomy may be used in short low strictures which are not due to neoplasms. (4) Benign neoplasms are removed. (5) Extensive strictures due to lye are best treated by esophagectomy and esophagogastric anastomosis, or, if limited, by resection and end-to-end anastomosis of the esophagus. (6) Malignant growths require esophagectomy and esophagogastrectomy with esophagogastric anastomosis. (7) Congenital atresias are treated by direct

identified if large. If small, the esophagoscope may be used to identify it. Local anesthesia is preferred if an endoscopist is not available because swallowing distends the sac, making it easy to see. Some surgeons prefer to do the operation in two stages so that in the event of leakage after removal of the sac, adhesions will prevent a mediastinitis (see Chapter 19). At the first stage the sac is freed and turned upward so that it cannot fill and is anchored to the skin. Two weeks later it is removed. We have used the one-stage technique routinely with excellent results.

Fig. 262.—Traction-pulsion diverticulum of the esophagus. X-ray photograph indicating a traction-pulsion type of diverticulum. The diverticulum is of the right lateral wall of the middle third of the esophagus which is a very common position. Although small traction diverticula and traction-pulsion diverticula of the esophagus may be symptomless and may not require surgery, it is probably wise to remove them if they cause symptoms or are known to be increasing in size. A third variety of diverticulum is sometimes encountered above the diaphragm. It has been referred to as epiphrenic or supradiaphragmatic diverticulum It is classed as a pulsion type. These are rare and the symptoms which they produce are very similar to those of cardiospasm. If they are increasing in size they should be attacked surgically. The cause of supradiaphragmatic diverticula is said to be linked with cardiospasm, and it is thought by some that it is the first sign of dilation following cardiospasm taking place in an abnormal way due to a weakness in one portion of the esophageal wall.

Thoracic esophageal diverticula are rare. They are of the traction or pulsion variety or both. The traction types are conical and result from adhesions to tuberculous lymph nodes as a rule. The mouth of the diverticulum is wide open so that food entering may leave, and therefore they do not produce symptoms except from perforations. As they enlarge, pulsion forces become active also. The pulsion type is said to result from

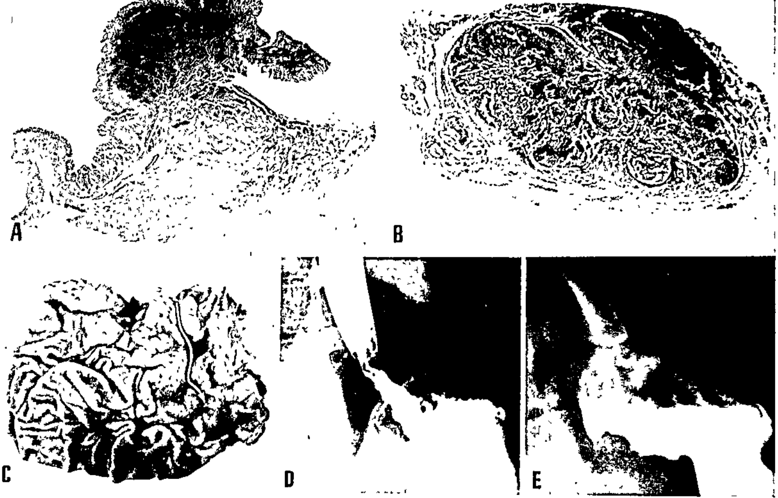


Fig. 264.—Carcinoma of the lower third of the esophagus. A. A. was a woman 46 years of age who complained of difficulty in swallowing solid foods and an oppressive feeling in the lower thorax. She had been sick for over a year and the dysphagia increased, until just before her admission into the hospital it was difficult for her to swallow liquids. She was operated upon through the bed of the seventh rib, and the lower end of the esophagus and upper end of the stomach were removed and an esophagogastrostomy was performed. *D*, X-ray photograph showing the neoplastic filling defect in the lower esophagus and the cardiac end of the stomach. *C*. Photograph of the gross specimen, with arrow pointing to the lesion in the esophagus.

anastomosis when feasible. If the defect is too extensive, the proximal end of the esophagus is brought out through an incision in the neck and gastrostomy is done. Later a subcutaneous esophagus is made by (1) a skin tube, (2) a segment of jejunum within the skin tube or the proximal end of the esophagus is later anastomosed in the neck as follows: (a) the stomach is brought up into the chest and anastomosed to the esophagus in the neck, and (b) a segment of jejunum is brought up into the chest after a Roux Y anastomosis to establish intestinal continuity.

Fig. 263.—Esophageal stricture with perforation. Patient was a woman aged 20 years with a congenital stricture. She had received repeated dilatations. Note the dilatation of the esophagus above the lesion. The arrow points to a perforation which was accidentally produced at the time of esophagoscopy.

Neoplasms of the Esophagus

Neoplasms of the esophagus may be benign or malignant, primary or secondary. The former include intramural fibroma, lipoma, fibrolipoma and fibromyxoma, leiomyoma, adenoma, and papilloma. They cannot be diagnosed by the history because dysphagia is common to all esophageal diseases. Pedunculated types may be regurgitated into the mouth. Fluoroscopy with barium meal and esophagoscopy reveal the true nature of the

For extirpation, the esophagus may be divided into four groups:

1. The upper fourth presents at present many technical difficulties. The extreme upper end may be removed in connection with carcinoma of the larynx and a permanent tracheotomy and esophagotomy done, or pedicle tube grafts may be fashioned and an external esophagus made connecting the hypopharynx with the cervical esophagus. A few cases have been reported. Below this, in the upper fourth resections may be done and the stomach or jejunum brought up into the neck for anastomosis.

2. The middle half of the thoracic portion of the esophagus when involved should be removed down to the cardia and then a high esophagogastric anastomosis done above and anterior to the aortic arch.

3. The lower fourth of the esophagus or fundus of the stomach may be removed for lesions in this area with esophagogastric anastomosis.

4. Lesions which involve most of the stomach and the extreme lower end of the esophagus require total gastrectomy and an esophagojejunostomy (or rarely esophagoduodenostomy) if the duodenum can be mobilized.

The approach for the extreme upper portion is through the neck. A collar incision which extends down as the perpendicular part of a T may be projected into the superior mediastinum.

For midthoracic resections the left eighth rib is resected (sometimes the seventh), and in addition the fifth and sixth ribs may be divided posteriorly. The incision may be carried down into the abdomen as far as necessary. The chest is opened and the resectability determined. Next, the mediastinal pleura is incised and the esophagus freed down to the hiatus. The phrenic nerve is crushed. The diaphragm is divided anterolaterally and the stomach mobilized, care being taken to leave the right gastric and right gastroepiloic arteries to preserve the blood supply to the mobilized stomach which is brought high into the chest for anastomosis. The esophagus through its lower portion, including the growth and a safe margin above it, is removed, the cardiac end of the stomach closed, and esophagogastric anastomosis done.

For the lower portion of the esophagus and for extensive stomach resections, a combined abdominothoracic incision is excellent. We have used an oblique one up through the bed of the eighth rib (or the eighth and ninth costal cartilages may be cut and an intercostal incision made). The abdominal incision is made first to determine operability. We have supplemented this with a feeding jejunostomy.

Other methods of anastomosis include the Torek operation. This consists of removing the esophagus, bringing out the upper end through an incision in the neck, and doing a gastrostomy. The two ends are joined by making a subcutaneous skin-lined esophagus at a second stage. An exteriorized loop of jejunum with one primary branch of the mesenteric artery and vein may be implanted under the skin. Later its blood supply may be divided and at a third stage the two ends joined to the distal end of the esophagus in the neck and the proximal end of the stomach below.

lesion. Treatment: Some intraluminal pedunculated polyps may be removed through the esophagoscope. Most will require local excision by transthoracic operation. If the entire circumference is involved, resection of the esophagus is necessary, with end-to-end anastomosis or, if extensive, with esophagogastrostomy.

Malignant growths include carcinoma and rarely sarcoma. Primary carcinoma of the esophagus is usually of the squamous-cell variety but may be an adenocarcinoma which has extended up from the stomach. The tumors often spread in the submucous and muscular coats for a distance of several centimeters, detectable only on microscopic examination. Metastases to regional nodes and even those below the diaphragm and neck are frequent. Metastases to the liver are late, whereas the lung may be involved because venous return from the high gastric and esophageal areas enters the systemic circulation directly without passing through the portal system. Secondary carcinoma of the esophagus may originate in the trachea, bronchus, stomach, larynx, breast, pancreas, testes, and other organs which cannot be identified from microscopic section and therefore are termed undifferentiated.

Primary carcinoma is by far the more common. It is squamous in 75 to 80 per cent, adenocarcinoma in 10 to 15 per cent, and undifferentiated in about 3 to 5 per cent. Grossly the tumors are scirrhous, medullary, or papillary types.

Symptoms and Signs: The disease is more common in males and usually in middle life, but may occur at any age from 20 to 85 years. The onset is so insidious that in most cases the growth is fairly well advanced when suddenly there is some difficulty in swallowing hard food. Later there is pain, weight loss, regurgitation with some blood; the dysphagia now is present with soft foods, then liquids. Finally there is complete obstruction with overflow, causing cough and, very late, hoarseness due to recurrent laryngeal nerve involvement.

The diagnosis is made conclusively by barium meal fluoroscopy and a biopsy taken through the esophagoscope. Operability may be predicted by the result of these examinations. If barium is seen to extend outside the esophagus, there is already perforation which has been temporarily sealed. The extent of the lesion and fixation of the esophagus is a clue. A constant boring pain in the interscapular region of the back, persistent fever, masses in the rectal shelf, nodular liver, enlarged nodes in the neck (which may be biopsied) all indicate, but do not prove, inoperability.

Treatment consists of radical extirpation of the involved portion of the esophagus for cure. In late cases not suited for radical resection palliation may be obtained by careful dilation or gastrostomy (Ssabanejew-Frank's technique) which is permanent and will not leak. X-ray treatment affords relief from pain and will occasionally arrest the disease in lesions of the upper fourth of the esophagus. Jejunostomy as a preliminary measure to resection has been of no help in our cases.

and splanchnic layers of mesoderm. Later the mesocardium attaching the heart to the anterior body wall disappears and the right and left limbs of the U-shaped cavity become confluent anterior to the heart, forming a large pericardial chamber.

The primitive coelom is divided into separate cavities as has been described in Chapter 10 by the formation of three membranes; the septum transversum which separates the pericardial and pleural cavities from the peritoneal cavity incompletely, the pleuropericardial membrane which completes the division between the pericardium and pleural cavity, and the pleuroperitoneal membrane which closes the pleuroperitoneal hiatus on each side of the diaphragm, separating the pleural cavities from the peritoneal cavity. This has been discussed in connection with diaphragmatic hernia. Thus the abdominal wall evolves into a structure composed of an internal layer of mesothelium, an outer layer of epithelium, and between mesodermal derivatives, muscle and fat.

THE ABDOMINAL WALL

The abdominal wall is made of fibrous and muscular layers. These are attached above to the thorax; below, to the pelvis; and behind, to the erector spinae muscles and the vertebral column. In front, the layers join in the midline, forming the linea alba. The outside of this wall is, of course, covered by skin; the inside is lined by the parietal peritoneum. In between these layers are (from without inward) the superficial fascia (Camper's and Scarpa's in the groin), the external oblique muscle, the internal oblique, and the transversalis muscle. The aponeuroses of these muscles unite on each side (linea semilunaris) to form a sheath for the large rectus abdominis muscle. The right and left rectus muscles, in their upper three-fourths (above the linea semicircularis, which lies at the level of the iliac crests) have separate sheaths including a posterior layer (formed by the split internal oblique fascia and the transversalis), but in their lower fourth have only the transversalis fascia forming the posterior layer. The rectus muscles contain lineae transversae, transverse fibrous bands, which are also produced by transverse incisions at the lower level, and anterior to the recti are the pyramidales, and at the upper, the muscle is inserted into the xyphoid and superficial surface of the seventh, sixth, and fifth costal cartilages. On its anterior surface and adherent to the sheath are three or four transverse tendinous intersections (inscriptiones tendineae), the lowest opposite the umbilicus. The posterior abdominal wall is made up of muscles and fasciae. The muscles include the psoas major and minor, the quadratus lumborum, and, in the pelvis major, the iliacus. The transversalis muscle and aponeurosis are extremely important for they give the abdominal wall great strength and must be dealt with carefully during abdominal operations. In addition, the direction of their fibers vary in different constitutional types (in the lateral type, the fibers run transversely in the upper abdomen; in the linear type, obliquely); then too, is fascia, which covers its deep surface, is continuous with the fasciae of the quadratus lumborum, psoas, and diaphragm, and (below the inguinal ligament) with the fascia iliaca, with which it forms the femoral sheath, enclosing the femoral vessels and canal in their passage behind the inguinal ligament. It is penetrated by the spermatic cord or round ligament, forming the internal spermatic or infundibuliform fascia (q.v.). It is lined internally by the peritoneum and aids in forming various supporting structures about the pelvis.

The blood supply comes from the internal mammary (off the subclavian) and through the superior epigastric (off the external iliac). These two anastomose, thereby connecting upper and lower limbs. In addition, the lower two intercostals, the lumbar, iliolumbar, and circumflex iliac arteries help supply the abdominal wall. Superficial branches in the inguinal region (superficial epigastric, superficial circumflex iliac, and superficial external pudendal) come from the femoral. Venous return above the umbilicus is by companion veins which ultimately enter into the superior vena cava and below the umbilicus through the inferior vena cava. Thus, venous return flows in two directions; that is, from the superior epigastric into the internal mammary vein into the subclavian and from the inferior epigastric into the external iliac. The superficial veins

A right thoracic approach has been employed by some surgeons who make an upper, left paramedian abdominal incision. The stomach is mobilized and a jejunostomy done. At a second stage, the right sixth rib is removed and the operation carried out through the right thorax.

Prognosis without surgery is obviously 100 per cent fatal. The operation mortality for lesions in the lower portion of the esophagus is about 15 per cent, for the mid-thoracic esophagus, about 20 to 25 per cent at present. These figures will be improved as techniques are developed.

The rate of curability is still low and the time interval in most cases is too recent to draw conclusions. As the technique of these operations are improved and the diagnosis is made earlier, more cures will be obtained. The patients are comfortable after resection and eat anything they wish. The large stomach in the chest does present complications such as dyspnea after eating, regurgitation on reclining, and cardiac irregularities. However, they are inconsequential as compared to complete esophageal obstruction with gastrostomy feeding. We have had one case of sprue following the operation which was controlled by high protein diet, vitamin B complex, liver, and iron therapy.

DEVELOPMENT OF BODY CAVITIES

In the earliest embryo, segmentation takes place with the formation of the blastula and the early bastodermic vesicle. During this stage there is no differentiation into layers. Such differentiation takes place later, and the three primary germ layers, ectoderm, entoderm, and mesoderm, are formed. From these layers all of the body tissues and organs are derived. The germ layers consist of an outer ectoderm, inner entoderm, and a cavity known as the archenteron. Between the ectoderm and the entoderm lies the single sheath of mesoderm which soon splits into two, the cavity between being the coelom or body cavity. (See Fig. 17, Chapter 3.) After the mesoderm splits, the outer layer, which is known as the somatic layer, with the ectoderm forms the somatopleurae or body wall. The inner splanchnic layer with the entoderm forms the intestinal wall or the splanchnopleure.

In embryos of 1½ mm. the coelom consists of a U-shaped pericardial cavity, the right and left limbs of which are continued below into the paired pleuroperitoneal cavities, which in turn extend out into the extraembryonic coelom. Later the splanchnic mesoderm and the somatic mesoderm are united at the level where the vitelloumbilical trunk courses to the heart, forming the septum transversum. This separates the ventral mesenteries which have been formed into an upper, or thoracic portion, and a lower, or abdominal portion. Above the septum the heart is suspended into the ventral mesentery which forms the dorsal and ventral mesocardia. In the ventral mesentery below the septum grows the liver. This portion of the ventral mesentery gives rise posteriorly to the lesser omentum of the stomach and with the septum transversum forms the ligaments of the liver. Anteriorly the ventral mesentery persists as the falciform ligament. Posterior to the gut, the splanchnic mesoderm on each side is folded together in the median saggital plane and constitutes the posterior mesentery which extends to the caudal end of the digestive canal. This mesentery suspends the stomach and intestines from the dorsal body wall and it is divided into the dorsal mesogastrium or greater omentum of the stomach, mesoduodenum, the mesentery proper of the small intestine, the mesocolon, and the mesorectum. The covering layers of the viscera of the mesenteries and of the body wall are continuous with each other and consist of mesothelium lying on connective tissue. They are derived from the somatic

The abdominal cavity has entrances and exits: the esophageal, vena caval, and aortic openings in the diaphragm; the umbilicus, which permitted the temporary exodus of the intestines during intrauterine life; the inguinal canal for the spermatic cord in the male and for the round ligament in the female; the femoral canal medial to the femoral vein, artery, and nerve; and the obturator and sciatic openings in the pelvic basin. These constitute congenital points of "least resistance" to intra-abdominal pressure, which may give rise to a protrusion called hernia.

Congenital Anomalies Involving the Abdominal Wall and the Umbilicus

Congenital anomalies which are more commonly encountered in the abdominal wall are the following: (1) cyst of the umbilical cord, (2) omphalocele, (3) patent urachus and urachal cyst, (4) peristsent vitelline or omphalomesenteric duct, (5) umbilical hernia, and (6) ventral hernia.

Cyst of the Umbilical Cord.—Cyst of the umbilical cord is in reality a collection of Wharton's jelly close to the abdominal wall. The obstetrician is loath to tie the cord, thinking that this cystlike protrusion may contain abdominal viscera. He usually ties distal to the cyst, which is proper. Sometimes the cyst is large and may interfere with delivery. As soon as the child has been delivered and after careful inspection, the cyst is removed. The condition is extremely rare.

Omphalocele.—Omphalocele has many symptoms. The malformation has been called funicular hernia of the umbilicus, hernia into the umbilical cord, umbilical eventration, amniotic hernia, exomphalos, and omphalocele, (3) patent urachus and urachal cyst, (4) persistent vitelline skin. It is in reality a herniation of abdominal viscera into the base of the umbilical cord. The covering of this protrusion is a thin translucent membrane which consists of peritoneum internally and portions of amniotic membrane externally. From previous discussions we have seen that between the sixth and tenth week of fetal life, a portion of the abdominal viscera is extruded from the coelomic cavity proper into the external coelom through the base of the umbilical cord. We have also seen that this probably occurs so that the space necessary for the great enlargement of the liver may be available. After the tenth week, the size of the abdomen is increased to such a degree that the organs begin to return and the abdominal cavity can accommodate them. However, if there should be any disparity in size between the abdomen and the size of the viscera, the intestines or the liver, or both, may continue to remain outside the coelomic cavity proper. It is our impression from the cases that we have seen that it is not the size of the liver or the intestines but rather the retarded development of the abdominal cavity that is at fault.

Pathological Findings.—The sac is thin and the intestines and the liver may be seen through it. Usually it varies in thickness in different portions, indicating that some parts of the sac are covered with amnion and other parts are covered only by peritoneum. The size varies. Sometimes the entire abdominal wall is deficient. The average size is about 6 cm.,

also follow this course. Last, from the umbilicus blood is carried into the portal circulation by the veins of the round ligament of the liver and in this way the abdominal wall circulation may be connected with the mesenteric.

The superficial lymphatics of the upper anterior abdominal wall drain into the axillary and those below the umbilicus into the superficial inguinals (Chapter 23). The deep lymphatics in the upper anterior abdominal wall drain into the deep axillary, and those below the level of the umbilicus into the deep femoral (via inferior epigastric and deep circumflex iliac trunks) and into the periaortic nodes by way of the trunks which follow the lumbar vessels.

The superficial lymphatics of the umbilicus empty into the axillary (upper half, and inguinal (lower half) nodes. The deep lymphatics drain into the deep axillary, anterior mediastinal (via internal mammary), deep femoral (via inferior epigastrics), and the periortic (via lymphatics which accompany lumbar vessels) nodes. From the deep femoral, lymph channels go to the iliac lymph nodes. Lymph channels are also found along the ligamentum teres (obliterated umbilical vein) which run in the porta hepatis to the liver; in the obliterated urachus to the bladder; and in the vitelline duct *if present to reach the intestines.*

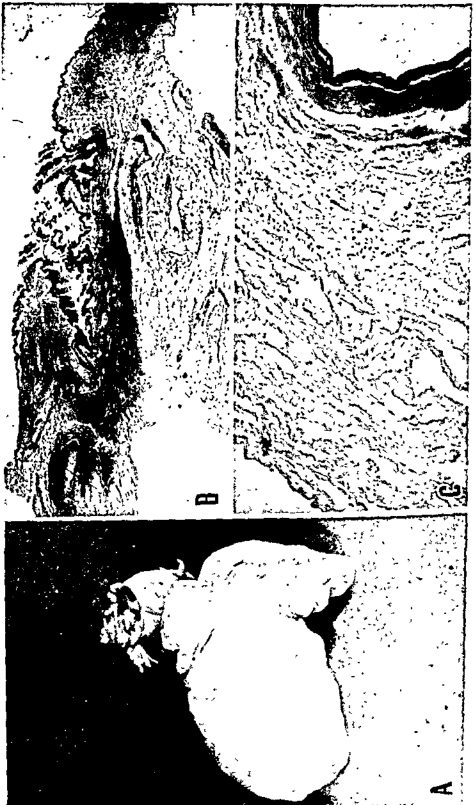
Small isolated nodes are found in the deeper fascial planes, recti muscles, and periumbilical extraperitoneal tissues. The latter are often felt in extensive intra-abdominal cancer. The linea alba has no lymphatics crossing it so that this median rape really divides the superficial (but not the preperitoneal) lymphatics into right and left halves; this is not true in the immediate vicinity of the umbilicus.

Rigidity of the abdominal muscles is a useful sign in diagnosing intra-abdominal and often intrathoracic lesions. It is also termed muscle spasm, defense, or splinting. The recti muscles have a bilateral cortical innervation and ordinarily one cannot be contracted without the other voluntarily. Localized abdominal rigidity as ordinarily elicited with one hand over an inflamed appendix is not really localized because if both hands are used, both recti are contracted as are the obliques. This is a voluntary protection on the part of the patient. If the unaffected side is palpated first, no rigidity is found; therefore the practice of using one hand and feeling the unaffected side first is good examining technique. If there is a peritonitis, a "one hand" examination reveals equal rigidity in both sides. Another illusion occurs when unanalogous parts of the abdominal wall are palpated because the recti have more tone than the lateral group of muscles. Last, a tumor mas may be at first thought to be rigid. Involuntary rigidity may arise from parietal peritoneum or parietal pleural irritation; also from thoracic or abdominal viscera disease without irritation of the overlying pleura or peritoneum. Since embryologically the enteron is a midline organ, rigidity caused by "visceromotor" reflexes is supposed to be bilaterally symmetrical. Distention of the hollow abdominal viscera or stimulation of the central end of the superior mesenteric nerve will cause contractions of the anterior abdominal muscles in decapitated animals. The objection to this hypothesis is not the existence of a visceromotor pathway, but rather the observation that the peritoneum or pleura responds to any stimulus as a whole rather than in segments, even in certain instances of acute myocardial infarction.

Since the nerve supply comes from the lower intercostal nerves on each side, incisions are made close to the midline, or in an oblique direction, in order to avoid injuring them, since injury to the nerves causes muscular paralysis and abdominal weakness. Even more important is the use of muscle-splitting or anatomic incisions, thereby avoiding the division of these structures. The abdominal wall is not only an enclosure for the abdominal contents but is also important for their protection, and, by the variations in intra-abdominal pressure which it may produce, helps the function of the abdominal organs as well as the function of respiration. The umbilicus is an important structure because it represents a landmark of important embryological events. It is of interest to the surgeon because of its relation to the portal circulation, liver, peritoneal cavity (umbilical hernia), urinary bladder (patent vitelline duct), the anterior mediastinum (by way of the lymphatics), and umbilical ligaments (obliterated umbilical vessels).

Fig. 265.—Omphalocele. *A.* Photograph of the gross specimen of an omphalocele removed from an infant 18 hours of age. This was small enough so that the mass could be removed and the layers of the abdominal wall closed in layers. *B.* Photomicrograph showing the transition zone between the skin and the omphalocele. *C.* High-power photomicrograph through the wall of the omphalocele which, as can be seen, is composed of peritoneum and amnion. In larger defects it may be hazardous to replace the contents of the sac because the intraabdominal pressure would be increased to such a magnitude that the diaphragm would be elevated and respirations could not take place fully. Also the venous return to the heart would be impeded. Therefore, Ladd has suggested that in such cases the contents be replaced and only the skin closed; then at a later date, when the abdominal cavity increases in size, the abdominal wall may be closed in layers. We have employed this method in several cases.

In very large omphaloceles it is, perhaps, best not to attempt to remove the sac but simply to close the skin over it if possible, leaving the omphalocele sac in situ. We have had success with this method. The operation should be done as early as possible because the sac is thin and soon becomes hard and friable and cracks and may cause peritonitis if delay is too long. It is best, wherever possible, to open the sac and examine the abdominal contents if this is consistent with the possibility of closure. If, however, the sac is so large that it cannot be removed, then wide undermining of the skin and closure of the skin over the sac is the desired method of treatment. The reason for exploring in the smaller sacs is that associated anomalies are frequently present, and, although the sac may be closed perfectly, atresias may be present within the abdomen which may result fatally.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not only because it permits better closure, but also because it enables the surgeon to discover other anomalies which may be incompatible with life. We have recently had two cases of this type with congenital atresias of the small bowel. The atresias were removed, lateral anastomosis done, and the abdominal defect closed.

Patent Urachus and Urachal Cysts.—In early embryos the bladder normally extends up to the umbilical region. The bladder subsequently descends along the anterior abdominal wall. During this descent, the upper part forms a tubelike structure, the urachus, which subsequently becomes obliterated. The urachus is derived from the superior part of the alantois.

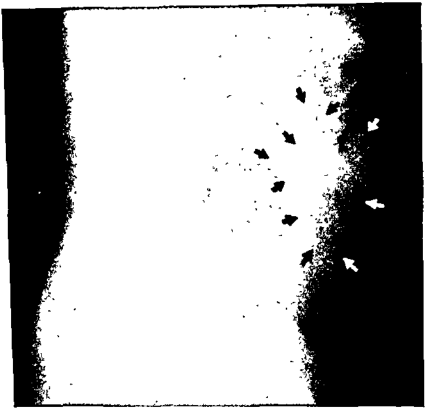

Fig. 266.—Urachal cyst. A persistent urachus is apt to manifest itself in one of four ways. It may be open at the umbilicus, permitting urine to flow from the bladder to the outside. This would be a urachal fistula. It may be closed at the bladder side but open at the umbilicus and become repeatedly infected. This would be a urachal sinus. It may be closed at both ends and this would constitute a urachal cyst. The danger of this cyst is that it may become infected and cause fever and all the symptoms and signs of inflammation. The fourth possibility is that the umbilical end may be closed and the bladder end open, in which case there may be a discharge of pus from an infected cyst giving rise to repeated attacks of cystitis. The lateral x-ray photograph shows a child 2 years of age (R. S.) with an infected urachal cyst. (Arrows point to the cyst.) This did not communicate with the bladder nor did it have an outside opening at the umbilicus. The patient was operated upon and the cyst was removed extraperitoneally, without complications. (Referred by Dr. H. Call.)

The symptoms and signs of a patent urachus vary with the degree of patency. If the entire urachal channel is open, there will be intermittent escape of urine through the umbilicus. If the cutaneous opening is patent

and the fascial opening is usually about 4 or 5 cm. in diameter. The skin of the abdominal wall may end abruptly or may grow irregularly over the top of the sac. This latter finding is important because it may mislead one into believing that the sac will be covered by epithelium. However, the blood supply of the sac is poor and soon it dies and shrivels and breaks and peritonitis sets in from leakage. Evisceration may occur and such cases are usually fatal. The symptoms and signs of this condition are also misleading because during the first day or two of life, the infant seems to be doing very well. The sac is so large that obstruction is rarely encountered. Like all congenital anomalies, the lesion rarely occurs singly and there are usually associated anomalies, such as imperforate anus, harelip, and even hydrocephalus.

Treatment.—The treatment of this condition is *immediate surgery*. The very large sacs are difficult to handle because there is not enough room within the abdominal cavity for the viscera and not enough skin to cover them over. If one waits until the abdominal cavity grows, the membrane will surely rupture and a fatal peritonitis will ensue. The best time to operate upon the baby is within the first 12 hours of life. If the sac is extremely large, the plan of procedure should be as follows:

The replacement of viscera should not be attempted in large omphaloceles. In our experience this procedure in itself will cause death on the table by pressure on the vena cava which prevents the proper return of blood to the right heart. The membrane is left in situ and the skin of the abdominal wall closed very loosely over it, leaving a gap of as much as is necessary in order to avoid too much tension. If the gap is inordinate extensive undermining of the skin of the abdomen and chest may permit closure or a split-thickness graft is taken from the mother, placed over the plicated opening, and held in place by the sutures in the skin margin. Later the graft dies, but valuable time will have been gained. We are aware that this is at best an incomplete procedure. However, it permits the tension on the sac to be released, thereby preserving this membrane for another few days. With this brief respite of time, the skin may be closed and the fascia is left open, thereby leaving a permanent hernia which is covered only by skin and peritoneum. Later, when the child is older, this large hernia may be closed. In the smaller types of omphalocele the procedure is that of the closure of any hernia; replacement of viscera, excision of the sac, and closure of the abdominal wall. The two umbilical arteries and umbilical vein are tied. This is not always necessary because there may be a blood clot in them, but it is our practice to do so. It is not always possible to dissect free the muscle and fascial layers, but if this is possible a better closure results. The peritoneum and posterior rectus sheath are closed; the rectus muscles are then mobilized so that they may be loosely approximated, and then the anterior fascia is dissected out and closed with interrupted stitches placed so the fascia will be overlapped if possible. Wherever possible, it is desirable that the sac be removed

can be done extraperitoneally, if it is done with care. Sometimes, however, the adhesions between the posterior wall of the cyst or fistula or sinus and the peritoneum are extremely thin. Every effort should be made not to violate the peritoneum. Should this occur however, the peritoneal membrane should be closed promptly. The fistulous tract is traced down to the bladder, it is divided and the bladder wall is turned in. The results are uniformly good and the mortality is extremely low.

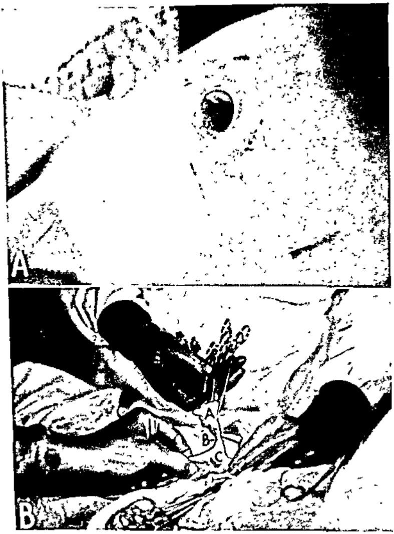

Fig. 267.—Meckel's diverticulum with patent omphalomesenteric duct. *A.* Photograph showing protruding and excoriated umbilicus of a 5-month-old boy. The child had had repeated hemorrhage from the bowel. The umbilicus was covered with a thin membrane, beneath which was clotted blood. *B.* Photograph at operation. (a) Umbilicus; (b) Omphalomesenteric duct; (c) Meckel's diverticulum. The tissue from the diverticulum contained gastric mucosa which was ulcerated. The operation resulted in complete recovery. (After Berman, J. K.: Internat. Clin. 4: 240, 1937.)

Persistent Vitelline or Omphalomesenteric Duct.—In our discussion of the embryology of the midgut, we shall see that the vitelline duct is an embryological structure which extends between the ileum and the yolk

and the epithelial lining ends blindly, there will be more or less mucoid secretion at the naval, and should this channel become secondarily infected as it usually does, there will be a recurrent episode of omphalitis with abscess formation. The patient usually refers to his "recurrent boils of the navel." Should there be no communication with the outside and no communication with the bladder, a cyst results which will be extraperitoneal. This cyst manifests itself as a swelling below the navel and it has a *definite broad attachment to the internal part of the abdominal wall.*

Urachal cysts are seen in infants and in adults. Sometimes the cyst suddenly increases in size. This is thought to be the result of an incomplete membrane separating the urachus from the bladder and this membrane suddenly ruptures. The history in most of our cases has been as follows: The child was perfectly normal until 5 years of age when a swelling occurred below the umbilicus. This caused the child to become very sick with chills and a high fever. Subsequently, a diagnosis of pyelitis was made because the *family doctor found a great amount of pus in the urine.* The child's symptoms quickly subsided, only to recur within several months. At operation a large urachal cyst with connection in the bladder was found. This, then, was a closed external opening and a patent internal opening forming a sinus which communicated not only with the skin but with the bladder. Urachal cysts frequently become infected because even though they have no internal or external communication; the endogenous bacteria multiply due to mild trauma or hemorrhage and cause an infection. In fact, frequently the diagnosis is that of a boil of the abdominal wall which is opened, and sometimes a cure results due to the fact that the infection has destroyed the wall of the cyst.

The diagnosis of urachal cyst is difficult to make if there are no openings. Lateral x-ray films sometimes help because no intestines will be found in the mass. A cystogram may show the distortion of the bladder. This may aid in diagnosis. If the urachus is patent to the outside, differential diagnosis must be made between a granulating umbilicus, which is nothing more than a small amount of granulation tissue left over after the cord has sloughed, and granulation tissue secondary to an omphalitis or a persistent vitelline duct. We shall discuss the latter in the next paragraph. The discharge from a persistent vitelline duct or omphalomesenteric duct is that of fecal matter rather than urine, or if the channel is lined with gastric epithelium, which it sometimes is, there may be hemorrhage due to peptic ulcer. Injection of Lipiodol into the fistula or sinus may help make the differential diagnosis. A cystogram helps in making the diagnosis using an iodized solution for visualization.

The treatment is comparatively simple. If an infection is present, this should be drained, and as soon as immunity has been established, the child should be given penicillin and streptomycin and the cyst or fistula or sinus should be removed. If the connection includes the umbilicus, it must be excised with the fistula or with the cyst. The entire operation

ment are uniformly good. As in other anomalies, the lesion does not occur singly and there may be other defects present.

Meckel's Diverticulum.—It is generally believed that in 2 per cent of normal adults some remains of Meckel's diverticulum are present. The literature is full of various reports concerning changes which may occur in the diverticulum or as a result of its presence. Heterotopias of the mucous membrane and associated glands, superficial and deep, may occur and become implanted in various portions of the alimentary canal. The esophagus, stomach, pancreas, common bile duct, and lung all are a part of the original entodermal canal and its derivatives in the 5 mm. embryo. This explains the possibility of heterotopia.

The various complications which may result from Meckel's diverticulum may be listed as follows:

1. Peptic group in which gastric mucosa is present with ulcer, hemorrhage, or even perforations. In this connection it is surprising how little gastric tissue is necessary to produce an ulcer.

2. Obstructive group which may give rise to intussusception, volvulus, bands and adhesions, contents of inguinal or femoral hernia.

3. Diverticulitis group which may be simple, acute, acute with perforations, and gangrenous or chronic.

4. Umbilical group which may give rise to fecal fistula, umbilical adenoma, or prolapse of intestine through umbilical fistula.

5. The tumor group which may be benign, malignant, or heterotopic tissue such as pancreatic tissue or embryonal rests.

6. Incidental group which contains normal intestinal structure.

Pathologic changes occur in one-third of the cases.

Intussusception of Meckel's diverticulum is a cause of about 6 per cent of the intestinal obstructions.

Associated anomalies in this group are said to be present in about 15 per cent. In our study of congenital anomalies of the rectum and anus, we found 56 per cent associated anomalies.

The prevalence of this congenital abnormality warrants inspection of the terminal ileum for possible Meckel's diverticulum in abdominal exploration.

Umbilical Hernia.—Umbilical hernia is discussed in connection with congenital anomalies of the abdominal wall because it is said to result from a muscular and fascial defect where the wall has been pierced by the blood vessels of the umbilical cord. The hernia is covered by peritoneum, subcutaneous fat, superficial fascia, and skin. The hernial ring usually has a firm connective tissue edge which is made up of the posterior rectus and anterior rectus sheaths and the transversalis fascia. The rectus muscle bellies are separated in the periumbilical region. However, they may be separated up to the ensiform, producing more or less of a protrusion due to the diastasis of the recti muscles. This is not uncommon in women who have borne children. Umbilical hernias are more common in girls than in boys.

sac, at the base of the umbilical cord. During early embryonic life the ileum communicates with the yolk sac. This opening gradually narrows down as the ileum pulls away. The yolk sac remains within the cord and the vitello-intestinal duct loses its connection with the intestine at about the 7 mm. stage. At the base of the omphalomesenteric duct a small diverticulum may persist. This is known as Meckel's diverticulum and is said to be present in from 2 to 3 per cent of normal persons. Usually this small pouch is not connected with the umbilicus. However, occasionally a cord of tissue which is a remnant of the primitive vitelline duct, connecting the ileum to the umbilicus, may remain. If this duct remains open, a fistula may result, running from the ileum at about eighteen inches from the ileocecal valve to the umbilicus. This opening will permit the egress of fecal matter from time to time. As in the case of the urachus, if the external opening should be closed, there may be a communication with the inside, in which case there would be a large diverticulum known as Meckel's diverticulum which would persist. If both ends are closed a cyst of the omphalomesenteric duct will result. This cyst forms an attachment to the intestine and also to the inner aspect of the abdominal wall. In fact, such a cyst is not far removed from a duplication of the intestine, and some observers have thought that many duplications arise in a manner similar to the mode of origin just described. Usually the sinus or cyst or diverticulum is uncomplicated. However, repeated infections may occur and inflammations result. The complications of this condition will be discussed later but should be mentioned here; namely, that sometimes there is an heterotopia of other tissues within the persistent vitelline duct. This tissue may consist of gastric mucous membrane or pancreas or other types of tissue. If gastric mucous membrane is found, it will secrete gastric juice and cause considerable digestion of tissue around the umbilicus, producing an ulceration with bleeding. If the tissue is present within the Meckel's diverticulum, hemorrhage may ensue just as in the case of bleeding peptic ulcer.

The diagnosis of a persistent vitelline duct can be made by the symptoms and signs which are usually very simple to detect in the true fistula because of the intermittent discharge of fecal matter. If there is great ulceration or digestion of tissue around the navel, again the diagnosis is more or less obvious. The cysts are more difficult to diagnose and the small fistulae are also hard to diagnose, particularly from an urachus, as has just been described. A small amount of Lipiodol may be injected into the tract, and if it finds its way into the intestine, the diagnosis is made.

Treatment consists of excision of the umbilicus together with the fistulous tract or with the cyst. The tract should be traced down to the ileum and the surgeon should make sure that a Meckel's diverticulum does not remain behind. The preoperative preparation of these children is important. We have been using Sulfasuxidine, 1/4 Gm. per pound of body weight. Sulfathaladine may also be used. The results of this treat-

dividuals are apt to keep on gaining and then a real problem arises. If the hernia is incarcerated and weight reduction may be pursued, this should be done. If the hernia is strangulated and if the bowel is viable at operation and the patient a poor risk, a herniotomy is the treatment of choice. This is done to increase the size of the umbilical orifice so that threats of gangrene are removed. At a later date, after weight reduction and symptoms have subsided and obstruction relieved, the hernia may be repaired. If strangulation has been present long enough so that the bowel is already gangrenous, exteriorized portions of the bowel should be drained by an enterostomy and a Miller-Abbott tube should be anchored. Then, at a later date, with adequate preparation with Sulfasuxidine, introduced through the tube and through the fistulous opening, the bowel should be trimmed away and lateral anastomosis should be done. The hernia defect may be closed at this time or at another stage if the patient's condition does not warrant a continuation of the operation. Therefore, we may see that umbilical hernia in a child is usually not difficult to care for, but in an adult, particularly in an obese adult, umbilical hernia may constitute a real problem.

Ventral Hernia.—Any protrusion through the anterior abdominal wall has been called ventral hernia. In this sense, umbilical hernia is also a ventral hernia. We have not chosen to include umbilical hernia within this term nor do we include the incisional hernias or postoperative hernias in this group. This leaves three types of ventral hernia which should be considered with the defects of the anterior abdominal wall.

1. The epigastric hernias. These are protrusions of the properitoneal fat which occur in the midline of the abdomen. Most of them occur above the umbilicus and are small. Many of them, however, assume importance and may have complications such as incarceration or strangulation. Epigastric hernias are more common in men than in women and may be easily recognized because they are above the umbilicus as a rule and therefore are not truly umbilical hernias. We have recently seen two cases of epigastric hernia with incarceration. Another name of the epigastric type of hernia is hernia of the linea alba.

2. The second of this group of ventral hernias include the ventral lateral hernias or the hernias of the linea semilunaris (Spiegel's) which arise at the outer edge of the rectus muscle. They are due to a developmental defect, or according to some of the observers, the point of least resistance may occur as a result of abnormal banding of the abdominal muscles. It is important that the surgeon be aware that immediately above and medial to the ordinary direct and indirect inguinal hernia, the hernia of the linea semilunaris may occur. Hernias of this variety usually occur as a result of a defect in the internal oblique. The external oblique and the transversalis are not likely to have the defects described. The hernia of the linea semilunaris, then, is a protrusion of fat with or

The size of the hernia, of course, depends upon the size of the defect. Some of them reach very large proportions. Sometimes the umbilical hernia will contain omentum, a knuckle of bowel, or a large amount of the intestines. In the child, this is rarely true. However, in the adult, particularly in the obese adult, the hernia may reach huge proportions and as the intra-abdominal pressure increases due to the obesity, loops of bowel may become firmly attached in the sac, and intestinal obstruction may ensue in spite of the large abdominal defect.

The treatment of umbilical hernia in the infant is adhesive strapping which will help many of the children. Approximately half of these children have a narrowing of the opening so that strapping is directly responsible for a spontaneous cure; not that strapping causes the cure, but as the individual grows and the rectus muscles constrict, the hernial sac is fused by the two layers of peritoneum growing together. Sometimes the same result occurs whether the umbilicus is strapped or not. However, if the two edges are held together, the chances for a spontaneous cure are better. Also, the strapping prevents bowel or omentum from getting into the sac and may prevent complications. Umbilical hernias which persist to the age of 4 years of age usually will not be cured spontaneously, particularly if they are more than 1½ cm. in diameter. These should be closed by operation. Also surgery is indicated in those in which repeated incarcerations occur or in which strangulation is present. Umbilical herniorrhaphy should be done by a transverse incision, transverse closure, or a vertical incision and a vertical closure depending upon which direction has the greatest diameter; that is, if the transverse direction has the longer diameter, the hernia should be closed in a transverse manner, whereas the reverse is true when the transverse diameter is short and the vertical diameter is long. Many surgeons believe in preserving the umbilicus by undercutting and lifting it up. This may be done with either type of incision. If the umbilicus is preserved, it is their contention that it saves the child embarrassment, and, of course, the cosmetic result is better. Since this does not in any way complicate the procedure, it is probably a point well taken. In the uncomplicated types of hernia, the flaps are dissected loose from the underlying muscle, the peritoneum, and fascia. The redundant peritoneum is imbricated or excised if it is large and closed with interrupted silk sutures. The fascial surfaces are then closed by overlapping in a transverse direction or a vertical direction as indicated by the diameters of the defect. The skin is then closed with interrupted silk sutures. The operation is simple and the results are excellent.

In complicated umbilical hernias many problems arise, particularly in adults and especially in obese individuals. If there are no reasons for surgery due to the immediate complications, the patients should be urged to lose weight so that the "right domicile" is re-established and so that the contents of the sac may be returned to the abdominal cavity. Where a small defect exists in obese people, this should be closed because such in-

taneously by the end of the first or second year unless the cord is too short. Should descent fail to occur, operation, with replacement of the testicle, should be done before the age of puberty. To stretch the cord, after all adhesions have been cut, a suture is introduced through the gubernaculum and tied to a rubber band anchored to the thigh.

Anterior pituitary hormone has been used to aid in testicular descent. Some cures have been reported. Since it is not a reliable method, and since a hernia may be present, surgery is preferable. The hernia which usually accompanies the cryptorchidism may be abnormal in that the sac will be placed between the oblique muscles, since the processus vaginalis does not protrude beyond the external abdominal ring (interstitial hernia). In ectopic testes the sac may be in the perineum. Often an undesirable premature maturity is induced with this hormone. Experience has shown that if the testicle is going to descend, it will do so spontaneously before adolescence. If this does not occur, surgery should be done. Intra-abdominal testes should be removed because of the incidence of malignancy.

The incidence of malignancy in the abdominal type of undescended testes is greater than in the normally placed organs. Various theories have been advanced to explain this. One of them is that the temperature in the abdomen is entirely too high for the functioning of the spermatogenic cells and that due to the lack of function, atrophy and degeneration results. The nonfunctioning organ is more "susceptible" to malignancy in this case than in other organs of the body (Chapter 15). This tendency is of sufficient importance to warrant removal of an abdominal testis.

Ectopic testis is really not a nondescended testis. The organ usually follows the attachment of the gubernaculum, and this may be abnormally placed outside the external ring over the pubic bone or the upper thigh or even within the perineum. Here, there is clearly no lack of descent but an ectopic placement. The term retracted testes means that the cord and its structures are long enough, but due to the normal strong cremasteric reflex, it may lie in a very high position. The testes should be replaced within the scrotum. The reasons for surgery are (1) cosmetic, (2) the psychological effect in a child who is apt to find that he is different from other children, (3) to avoid trauma and injury if the organ lies beneath the skin and is exposed, (4) to avoid predisposition to malignant degeneration, since the abnormally placed organs have a diminished spermatogenic function leading to atrophy and degeneration.

Two rare conditions within the testes should be mentioned here. First, *torsion of the testis* which occurs occasionally as a result of a sharp blow and sometimes without any apparent cause. Torsion produces great pain and tenderness, nausea and vomiting, and swelling within the organ. The clinical symptoms and signs resemble those of an epididymitis which is gonorrheal in origin. However, it may be dis-

without intra-abdominal contents, coverings of which are peritoneum and the herniated fat and the external oblique fascia, which may also be thinned out, and the skin.

3. Lumbar hernias are included in the group known as ventral hernias. These occur between the crest of the ilium and the costal margin. Usually they are seen on the left side. The reason for the occurrence of lumbar hernias is difficult to explain except that above the middle of the crest of the ilium there is a small triangular space which is formed by the edge of the external oblique in front, the latissimus dorsi behind, and the crest of the ilium below. The floor of this triangle is formed by the internal oblique. The older anatomists called this the triangle of Petit or the trigonum lumbale. It forms a weak point in this region in which collections of pus pool or more rarely ventral hernia may occur. Above and a little posterior to the Petit triangle is another triangular space known as the fascial triangle. Its base is the twelfth rib. Anteriorly its wall is the posterior edge of the internal oblique and posteriorly the outer edge of the quadratus-lumborum forms its boundary. The lower portion of the kidney lies immediately beneath it, and the latissimus dorsi is pushed backward. The external oblique must be pushed forward in order to uncover this triangle. Two important nerves cross it; namely, the iliohypogastric and the ilioinguinal. Through these anatomical weak spots, hernia sometimes occurs. Strangulation or incarceration is extremely rare in such hernias. The defect is uncomfortable and annoying at times, especially when the patient coughs or sneezes, because there is a perceptible bulge whenever intra-abdominal pressure is increased.

Ventral hernias are repaired by imbricating the sacs and employing whatever fasciae are available and overlapping them. Sometimes the ingenuity of the surgeon is taxed in an effort to find suitable fascia to use. In such instances, a fascial graft may be necessary. Usually, however, by mobilization of the adjacent fascia the defect may be satisfactorily closed. However, the lumbar types are particularly difficult to cure.

Undescended Testes (Cryptorchidism).—The testis grows from the genital ridge on the posterior wall of the abdomen behind the peritoneum and anterior to the transversalis fascia. By the seventh month of intrauterine life it starts its descent, directed by the gubernaculum testis, which is a fibromuscular band of tissue at the inferior pole of the testis. By the eighth month the testis is in the inguinal canal, and by the ninth month it should be in the scrotum. Sometimes the testis is arrested in its descent, or fails to move from the abdomen, or is attached at vicarious sites. These abnormally located testes (cryptorchidism) are usually associated with a hernia. In certain lower animals, such as the bat and the elephant, cryptorchidism is normal. Many infants are born with the testes in the inguinal canals. These usually descend spon-

peritoneum and other layers with it; these form the snug covering of the cord. Should the opening fail to contract or remain open (as is normal in the rabbit), a hernia will develop. Other etiological factors are sudden increase in abdominal pressure, failure of the "inguinal shutter" (external oblique and the internal oblique and the transversalis), congenital absence of falx aponeurotica inguinalis, short and less oblique inguinal canal with external and internal rings more or less over each other—in this sense congenital predisposition. Intra-abdominal pressure forces viscera into it. Acquired (direct) hernias occur after operations and from strain and may occur even in the inguinal region. The mere

Fig. 269.—Huge right-sided indirect inguinal hernia, as shown by x-ray after a barium meal. The scrotum hung to the level of the knees and contained almost the entire intestinal tract. The patient was 35 years old and weighed 205 pounds. He had had the hernia for about twenty-seven years and had been unable to reduce it for fifteen years. Weight reduction of fifty-five pounds and gentle manipulation performed daily by the patient in the recumbent position finally resulted in a reduction which was almost complete before surgery. At operation the vaginal type of congenital hernia was found and was successfully repaired.

presence of an enlarged opening does not constitute a hernia, even though it may have such potentialities, for there is no protrusion of peritoneum. Such a protrusion is called a sac. The contents of this sac may vary greatly in different types of hernia and at different times. If it contains omentum, it is known as an epiplocele; if intestines, an enterocele; if peritoneal fluid alone is present, a cystocele. However, almost any organ may be in the sac, so that the surgeon must be on his guard lest he injure it. For example, the bladder, the appendix, the

tinguished from this by a careful history, thorough examination, and urethral smears. The condition requires immediate operation in order to prevent gangrene. Should the testes be destroyed, orchidectomy is necessary. Still more rare is a *torsion of the appendix testis* or the hydatid of Morgagni. This is a remnant of the degenerated Müllerian duct as described in Chapter 23. Should this become twisted on its pedicle, a similar condition of swelling and tenderness would occur. The diagnosis between this and the torsion is difficult and is usually not made until time of operation, when the twisted remnant is removed.

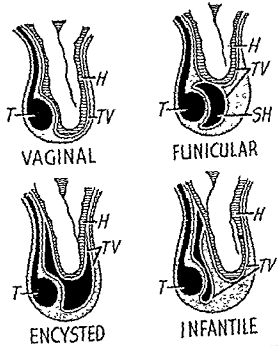

Fig. 268.—Types of congenital inguinal hernia. *T*, testicle; *H*, hernia; *T.V.*, tunica vaginalis, *S.H.*, site of hydrocele. The testis is originally an abdominal organ. By the third month it lies in the iliac *fossa*; by the *seventh month* at the internal abdominal ring; it is usually in the scrotum before birth. This descent is due to the unequal growth or active shortening of the gubernaculum. Preceding this descent a pouch of peritoneum (processus vaginalis peritonei) grows downward through the anterior abdominal wall, carrying a covering from each of the layers through which it passes. The testis originally lies behind the peritoneum and consequently descends posterior to this process, which becomes the tunica vaginalis. The visceral part is closely adherent to the testis, whereas the parietal part lines the scrotum (cf. the peritoneum and the pleura). The tunica vaginalis normally is obliterated from the internal abdominal (funicular) ring to the scrotum. Rarely, a rudimentary cord of tunica persists in this region. Should the vaginal process fail to close, a vaginal type of hernia occurs. If the funicular ring closes at a lower level, a hernia exists *above* and a hydrocele may develop *below* the occlusion. If the lower portion does not contain fluid, the funicular ring is invaginated into the part below (encysted type); or it may push down in *front* of the lower portion of the tunica (infantile). (Modified from Davis: Applied Anatomy.)

The word *hernia* is said to come from the Greek word meaning a branch. As used here, it may be defined as a protrusion of peritoneum, congenital or acquired, with or without visceral contents and covered with skin. There may be a protrusion from the abdomen not covered by peritoneum or skin which is known as evisceration. Most hernias are caused by a congenitally preformed protrusion. This is easy to understand in the inguinal hernias, for the testis is originally an intra-abdominal organ and must descend into the scrotum. In doing so it drags the

anisms may be active in those sliding hernias associated with mobile cecum and sigmoid. It is important to recognize sliding hernia because the surgeon may injure the cecum or the bladder or the sigmoid in an effort to tie off a sac which is really composed partly of bowel wall.

The treatment of this type of hernia is extremely difficult, because the peritoneum cannot be dissected off of the viscera. Many types of repair have been advocated for it. The most popularly accepted type is that described by Zimmerman and Laufman, who advocated dissecting the sac loose from the cord, pushing it back behind the transversalis fascia, and then closing this fascia tightly around the cord and doing a herniorraphy. It is not necessary in this maneuver to open the sac. It has been the custom to imbricate the sac by silk sutures, using an accordian pleat technique. Some authors have advocated dividing the spermatic cord and dropping the central end back into the properitoneal space and completely closing the canal. This is the best method of curing sliding hernia.

Hernias occur in many places and each has its anatomic peculiarities. Inguinal hernia may be direct and, if so, it is usually acquired. It is seen in obese men, 40 years of age or more, and comes through Hesselbach's triangle, medial to the inferior epigastric artery. The triangle has as its medial border the lateral edge of the rectus muscle and is divided into an inner and outer compartment by the obliterated hypogastric artery. If the direct hernia protrudes through the medial side of this structure (internal inguinal fossa), the coverings will be peritoneum, properitoneal (bladder), fat, transversalis fascia, falx inguinalis, aponeurotica, and external spermatic fascia and protrude medial to the external ring. If it protrudes through the middle inguinal fossa (lateral to the obliterated hypogastric), which is the common site, the coverings are the falx inguinalis and external spermatic fascia, and it protrudes through the external ring. If very close to the inferior epigastric, the cremasteric fascia instead of the falx covers it. It may be indirect and is usually due to a congenital defect (lateral to the deep epigastric artery), coming out through the external inguinal ring in the male (or less commonly in the female), or it may protrude lateral and mesial to the epigastric vessels (saddle or pantaloon hernia). Femoral hernia is a protrusion into the femoral canal, which normally is filled with loose areolar tissue. Its coverings are peritoneum, subperitoneal tissue (septum crurale), and transversalis fascia (femoral sheath) and makes its appearance at the saphenous opening if it descends this far, being covered by the cribiform fascia, subcutaneous tissue, and skin. It is more common in women than in men, but inguinal hernia is seen in women more frequently than the femoral type. Umbilical hernia occurs at the umbilicus. This has been described earlier in the chapter. Postoperative incisional or ventral hernia may occur wherever an incision has been made. This is usually seen after infected wounds (see Chapter

tubes, the ovaries, the colon, and sometimes most of the gastrointestinal tract may be in the hernial sac. The coverings of a hernia may vary in different regions. For example, in incisional hernia, peritoneum, superficial fascia, and skin may be the only layers present, whereas in the inguinal region the congenital hernia pushes before it all of the tissues that the testes brought down: peritoneum (processus vaginalis), extraperitoneal fatty tissue (areolar fatty tissue), transversalis (internal spermatic or endo-abdominal or infundibuliform), internal oblique and external oblique (cremasteric), external oblique (external spermatic or intercolumnar), superficial fascia, Camper's (fatty) and Scarpa's (membranous), and skin.

If the hernia may be replaced into the abdominal cavity, it is said to be *reducible*; if it cannot be replaced, it is *irreducible*, or *incarcerated*; in this type the blood supply is not impeded, but the function of the organ (for example, the fecal current) may be, in which case there results a bowel obstruction. Rarely, the sac and contents become *inflamed*, due to infection. This is dangerous because of the possibility of peritonitis. Should the intestine within the sac be irreducible and should its blood supply as well as its function be impaired, the hernia is said to be *strangulated*. Obviously, the danger of this situation is gangrene of the bowel, with perforation in addition to intestinal obstruction. There are also some special varieties of hernia; for example, a partially strangulated loop of bowel (Richter's hernia), a hernia of Meckel's diverticulum which forms a small pouch off of the ileum (Littre's hernia), and a sliding hernia (incomplete sac with the bowel forming part of it).

Sliding Hernia.—The term sliding hernia has been applied to two varieties, the more common of which is designated as the parasaccular or partial extrasaccular variety. This type corresponds to the pulling mechanism theory advanced many years ago. This is really not a sliding hernia as popularly described. It is seen in large indirect hernias which, as they increase in size, make traction on the parietal peritoneum and ultimately on the visceral peritoneum until some portion of retroperitoneal viscera, usually the cecum or descending colon, is drawn into the sac. If the hernia is a direct hernia, the posterior wall, instead of being made up of bowel, may be made up of bladder. The second type which is much less common, but which is the type popularly known as sliding hernia, is the extrasaccular or sacless hernia. This variety is due to a pushing mechanism, and in this type the viscus, together with the peritoneal covering, is pushed directly through the hernial orifice. This kind of sliding hernia cannot occur in indirect hernias if the saccular explanation for the genesis of oblique inguinal hernias can be accepted. It is possible, however, for such hernias to protrude through direct hernial orifices, and herniation of the bladder is not infrequent in this type of hernia. Since the pulsion type probably occurs in indirect hernia also, it is likely that both mech-

(Poupart's) ligament; in femoral hernia, at the femoral canal (saphenous opening), below the inguinal ligament and on the anteromedial aspect of the thigh; in umbilical hernia, at the umbilicus; in incisional hernia, at the site of the incision, etc. The obturator variety appears on the medial aspect of the thigh and the sciatic below the gluteus maximus muscle. Diaphragmatic hernias are usually discovered by x-ray studies but may first manifest themselves by partial obstruction of the stomach or bowel.

Fig. 270.—Diagram illustrating a type of internal hernia proximal to the cecum, one of the so-called paracecal varieties. The hernial sac was formed by the mesentery of the terminal ileum, cecum, and lower portion of the ascending colon. The orifice was about 5 cm. in diameter. The contents were mostly ileum. The angulation of the ileum produced an acute intestinal obstruction. This illustrates, then, a hernia into the mesentery of the terminal ileum and a persisting ascending mesocolon.

Complicated types of hernia present, in addition to the above, special symptoms and signs. The irreducible type presents a swelling which is painful and cannot be reduced; the strangulated type has, in addition, all of the symptoms and signs of acute intestinal obstruction. Although the rare inflamed variety may cause obstruction, the outstanding symptoms are heat, redness, and tenderness over the protrusion.

The treatment of hernia depends upon the age and general condition of the patient and the pathological variety present. Palliative treatment in the uncomplicated case consists of reduction of the hernia and its retention by a mechanical device such as a truss. In infants a pad held

3) or in badly debilitated individuals in whom repair is extremely slow. It is usually prevented by making incisions parallel to the fascial and muscle fibers, as in the McBurney incision, although inguinal hernia follows this incision more often than could be called coincidental. Some have thought this due to injury of the ileoinguinal and ileohypogastric nerves, but there is no proof of this. Rarely, an incisional hernia in the lower abdomen may protrude through the inguinal canal. McBurney incision hernias are rare unless there has been drainage and infection. Occasionally the surgeon will encounter an epigastric hernia, due to a congenital weakness between the recti muscles in the epigastrium, or a hernia through the linea semilunaris, and, more rarely, a hernia in the lumbar region through Petit's triangle. Also rare are those hernias occurring deep in the pelvis—through the obturator foramen (which permits exit of the obturator vessels and nerve) and through the sciatic foramen (which allows for the egress of the sciatic nerve). The diaphragm is occasionally the site of hernia. This has been discussed in Chapter 19. Accidental wounds in the diaphragm may cause an acquired type of hernia also. Internal hernia occurs as a result of congenital defects in the mesentery, or abnormal openings, or enlargement of normal foramina and is usually encountered about the duodenum or cecum.

Internal Hernia.—Internal hernias are due to congenital defects within the abdomen which may cause an intestinal obstruction and should be remembered in intestinal obstruction which cannot be readily accounted for. The sites for these hernias are as follows: (1) left mesenterico-parietal; also called paraduodenal hernia. The opening is below and to the left of the duodenojejunal juncture and leads behind the descending mesocolon and the descending colon. (2) Right mesenterico-parietal or paraduodenal hernia. The opening is below and to the right of the duodenojejunal juncture and leads behind the mesentery and possibly behind the ascending colon. (3) Defect in the mesentery, about the terminal ileum. (4) Hernia into the ascending mesocolon. (5) Defects in the omentum. (6) Defects in the broad ligament. (7) Herniation through the gastroepiploic foramen into the lesser peritoneal cavity. Of this group, Numbers 1, 2, 3, and 4 are uncommon, but important. Number 3 is perhaps the most common type.

The treatment is exploration, release of the obstruction if possible, and, if the bowel is gangrenous, resection with anastomosis. The aperture should be closed.

The sign of uncomplicated hernia is a soft protrusion or swelling which is slightly painful at times. This bulge is increased on standing, straining, or coughing and disappears when the patient reclines. By examination the surgeon can feel the opening and push the protrusion back with his finger. This soft swelling appears at the anatomic site of the hernia; in inguinal hernia, at the inguinal ring above the inguinal

cerning cotton and silk, tantalum and other kinds of wire. It is our opinion that a nonabsorbable suture should be used, although small catgut, which is chromacized, will do as well if the proper technique is observed. Recently, the use of preserved heterogenous grafts of fascia have been advocated. These grafts of fascia when transplanted into living human tissue have been observed to remain viable for a period of years. Such fascia is gradually replaced by the ingrowth of fibroblasts, capillary loops, and the formation of human connective tissue. This takes place over a period of years. Also, the use of patch fascial grafts for very large hernias has been advocated. The patch graft is a transplantation of a large section of fascia lata sewed into the defect in the abdominal wall. We have used this method occasionally and found it extremely valuable in very large postoperative hernias where there is insufficient adjacent fascia to use. A third type is that of a pedicle fascial graft in which the upper end of a graft is left attached to the fascia lata and the distal end is swung into the abdominal wall defect. It would seem that such a pedicle would carry very little blood supply, if that is the purpose of it, and therefore would have no advantage over a free transplant.

Last, the fascia may be used as suture material according to the methods advocated by Gallie. This material is said to live and form a permanent type of fascia. Still other methods of repair have been advocated. The method of McVey, which employs Cooper's ligament instead of the inguinal ligament, is an excellent suggestion. However, the older surgeons employed this ligament as well as the periosteum of the pubic tubercle in an effort to completely close Hesselbach's triangle.

The general rules for the repair of hernia includes the principles of wound healing as emphasized in Chapter 3. These consist of the following: (1) Careful dissection of the protruding sac should be done. (2) There should be complete obliteration of the sac, either by extirpation or imbrication. (3) The defect in the body wall should be covered by adjacent tissue if possible; that is, by mobilization of this tissue so that tension will not be present on the suture line. This has been discussed previously in Chapter 3; also wherever the discussion of suture has been mentioned within the text. (4) Sutures should not be tied too tight so that they strangulate the tissue. If all the factors considered in wound healing are carefully observed, good results will follow the repair of hernias. (5) The use of fascia has its place and it is perhaps most useful in the very large types of hernia in which no degree of mobilization is possible to close the defect. In such cases, however, if fascia should fail to take, some men have advocated epithelial transplants of skin. We have not used this method because of the danger of malignant degeneration of the misplaced squamous epithelial cells. (6) Last, very large defects may be closed in stages. We have frequently employed this method in the repair of postoperative hernias, closing

by an elastic belt may be used. The complicated varieties usually require operation, and if strangulated or incarcerated (with intestinal obstruction), this must be done immediately to save life. Occasionally in children or adults an incarcerated hernia is reduced so that operation may be deferred for a more favorable time. This is not without danger because the injured bowel may be ruptured, or, due to the trauma of reduction, may become gangrenous. Sometimes the protruding mass seems to be reduced when in reality it has simply been displaced under the deep fascia (reduction en masse). This obviously does not relieve obstruction. If an immediate operation is not practicable, the patient may be placed in a warm bath and urged to attempt gentle reduction himself. This is useful only in hernias of long standing where the patient has done this many times and has, by experience, learned how to accomplish it. An analgesic to relieve the intense pain may help him. Should reduction fail, operation is imperative. Injection methods of treatment which attempt to obliterate the sac by the introduction of sclerosing substances are advocated by some surgeons. However, this method is dangerous and ineffective—the former, because of injury to the bowel, blood vessels or peritoneum; the latter because the best that results is a large amount of scar tissue which subsequently stretches.

Operation is the method of choice for the permanent cure of hernia; the sac is completely extirpated and, in the case of inguinal hernia in the male, the inguinal canal is reconstructed; in hernias other than of the inguinal type, the canal is occluded. Silk or linen sutures are used. In very large hernias the sac wall is used to reinforce the wall of the abdomen. In extremely obese people it is well to defer operation until weight reduction has been accomplished. Other possible contraindications are in extremely large hernias where the intestines have been out in the scrotum for years and have, so to speak, "lost their right of domicile," although even these, after weight reduction, may be cured by operation. In patients with a chronic cough, there is apt to be dehiscence of the wound. Ascites, in addition to its mechanical disadvantage, usually implies a cirrhosis of the liver or other debilitating condition. Extreme youth does not in itself constitute a contraindication to surgery, but when inguinal hernia occurs in the newborn, because of the delicate structure of the sac and the spermatic veins and the liability to postoperative infection in infants due to soiling, operation may be deferred until the child is 4 or 5 years old. Because of the great tendency to incarceration in infants, we are now operating upon hernias much earlier than formerly, often immediately after birth. In late strangulated cases the treatment may have to be directed entirely to the obstruction (enterostomy, resection with double barrel enterostomy, q. v.) and the hernial repair done later.

Special Types of Repair.—*Much has been written recently about the* special qualities of different types of sutures. Particularly is this true con-

has been prepared for surgery. This consists of decompression with a Miller-Abbott tube at once or at least a Levine tube with suction, and restoring the electrolytes, giving transfusions of plasma or whole blood. If the patient is in a serious condition and the bowel is gangrenous, it is perhaps well to simply introduce a tube into the gangrenous loop and allow it to remain exteriorized. The Miller-Abbott tube will deflate from above. After the patient has recovered from this procedure, in seven to ten days, a second operation should be done with resection, anastomosis, and closure of the hernia. These patients are prepared with sulfasuxidine and the results are uniformly good.

(2) Umbilical hernias in obese individuals. The bowel may be incarcerated yet not strangulated. Such patients are poor surgical risks, yet it is imperative that immediate action be taken in order that the viability of the bowel be preserved. In such cases a simple herniotomy is done, increasing the size of the hernial opening and thereby relieving pressure on the incarcerated loop of bowel. Later, when the patient is greatly improved (within ten days to two weeks), the herniorraphy may be done in the routine manner. In dealing with any type of abdominal hernia, the fasciae which line the abdomen and pelvis should be looked upon as continuous layers. The transversalis fascia is not limited to the inner surface of the transversus abdominus muscle but is continuous with the intrinsic fasciae of the other components of the abdominal wall.

Injuries to the Abdominal Wall

Injuries to the abdominal wall are of importance chiefly because of the danger of injury within the abdomen. Incised wounds, lacerated wounds, contused wounds, and punctured wounds occur on the abdominal wall as elsewhere in the body. Contused wounds need some amplification. As a result of a contusion, there may be a hematoma. This may cause swelling, induration, pain, vomiting, and rigidity. These symptoms may so mimic intra-abdominal injury that it may be difficult to determine whether or not there has been injury within the abdomen. Sometimes injuries of the abdominal wall occur spontaneously. This is particularly true in pregnancy, during labor, or after debilitating disease, particularly typhoid fever. Here the injury is usually in the lower abdomen, and a hematoma may form as a result of a tear in the epigastric vein or artery. Rarely these vessels may be torn, together with muscle tears, in violent exercise. Any of these injuries may cause symptoms which resemble those of intra-abdominal injury. It should be said in summary that contusions and injuries to the abdominal wall are important not only because of their intrinsic damage, but also because of what may be present in the abdomen.

Injuries to the abdominal wall may be produced by the following: (1) External factors. These may be single or multiple and may be listed as follows: (a) penetrating wounds caused by pins, knives, daggers,

one-fourth to one-half of the opening at one time and then proceeding to close from each end until the entire area has been approximated.

Recurrences Following Repair of Hernias.—Recurrences do occur. The incidence is variously estimated as 2 to 8 per cent. Factors which contribute to recurrence may be listed as follows: (1) The body build of the patient. This would include very poor musculature, the poor development of the falx aponeurotica inguinalis, stretching out of fascial structures, the length of the canal (that is, the short canal with superimposed rings is more liable to recurrence). (2) Systemic factors, such as anemia, great weight loss, general debility. (3) Local factors. These are probably the most common offenders and they include infection in the wound, the breaking of sutures, perhaps due to insertion of the sutures under tension, failure to obtain fascial approximation due to the interposition of fat areolar tissue, the failure of complete removal of the sac, the presence of a hematoma, and nerve injury resulting in muscular weakness. Complications such as postoperative cough, abdominal distention, and direct trauma play a role. (4) Miscellaneous local causes—bilateral one-stage operations in which tension is placed on one side and at the same time on the other. This may result in a pull toward the center from both directions, putting a stretch on the suture line. In large hernias the intra-abdominal pressure may be too great. Also something else should be said about double operations in one stage. Unless the surgeon is extremely careful, he is apt to do one side and then more or less hurry through the other side, leading to incomplete work. It is better in large hernias especially to do one side at a time and this is our practice, except in children. Among local factors that should be mentioned is an unrecognized direct hernia. Usually the indirect component is recognized, but the direct part of the hernia has not been repaired. In the Halstead type of repair, where the cord is transplanted beneath the superficial fascia, the internal ring may lie directly beneath the external ring unless the surgeon is aware of this difficulty. In that case, recurrences are very apt to occur. It has been our practice when using this type of repair to be sure that the two rings are not superimposed one on the other.

The type of work that an individual does has been used as an explanation for recurrence. This is particularly true of those who do heavy lifting. Some observers have stated that the practice of getting patients out of bed too early after surgery may play a role. It is our custom to permit our patients, particularly male patients, to stand up to void as soon as there is an urge to urinate, and we do not consider early rising in any form as a cause for recurrence. In fact, recurrences have been decreased since the practice of early mobilization of the patient has been invoked.

Complicated Hernias.—(1) The most common of these is a strangulated loop of bowel. Operation should be done as soon as the patient

has been prepared for surgery. This consists of decompression with a Miller-Abbott tube at once or at least a Levine tube with suction, and restoring the electrolytes, giving transfusions of plasma or whole blood. If the patient is in a serious condition and the bowel is gangrenous, it is perhaps well to simply introduce a tube into the gangrenous loop and allow it to remain exteriorized. The Miller-Abbott tube will deflate from above. After the patient has recovered from this procedure, in seven to ten days, a second operation should be done with resection, anastomosis, and closure of the hernia. These patients are prepared with sulfasuxidine and the results are uniformly good.

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Injuries to the abdominal wall may be produced by the following: (1) External factors. These may be single or multiple and may be listed as follows: (a) penetrating wounds caused by pins, knives, daggers,

screw drivers, etc., (b) perforating wounds caused by bullets or shrapnel, (c) wounds caused by blunt trauma (this is particularly true in automobile accidents), (d) wounds caused by immersion blasts, (e) wounds following surgery (by this we mean dehiscence or evisceration). (2) Internal factors. These are seen in cases of air introduced into the rectum, usually as a prank, followed by direct results, with perforation of the large intestine. Internal injury may also be caused by immersion blasts in which case it is assumed that water is forced into the anus, causing a rupture of the large intestine only. This has been called hydraulic abdominal concussion. A word should be said in connection with immersion blast. The subject has been reviewed in Chapter 12. It will be recalled that the force transmitted by an explosion in the water is four times that in the air. Usually it affects the abdomen because the victim is swimming in the water or is being held up by a life belt. However, injury to the lung may also occur unless the victim is swimming on his back. Consequently during World War II, sailors were advised to swim on their backs as much as possible and to stay out of the water as completely as they could by hanging to life rafts. The injury produced may be severe, including wide tears and lacerations and hemorrhage. The bowel may be completely torn in two.

The abdomen may be injured by penetrating or perforating wounds at any level, namely, in the epigastric, umbilical, or in the pelvic region. However, injuries of the abdomen can take place through the chest or through the buttocks. Consequently, it must be always borne in mind that the important thing is not the site of entrance, but the path which the penetrating or perforating objects have taken. This may involve the abdomen or parts of the chest or both. This has been particularly true in wounds of the buttocks by bullets which may penetrate into the lower abdomen, causing trauma to the bowel and hemorrhage in the abdomen.

Pathological changes: The pathology in wounds of the abdomen may be divided into general and local. The former includes shock and septicemia. The latter includes the local damage to the organ or organs by the object. There is an old dictum that wounded men die from hemorrhage, shock, or infection. The first two hours death is due to hemorrhage, and the first two days it is due to shock, but the shock is caused usually by hemorrhage. Later it is from infection. Bearing this in mind, the general pathological changes will be those which are incident to hemorrhage or to infection with dissemination.

Very often the injury to the bowel or to the solid viscus is not complete. This is particularly true of the bowel wall. The bowel may be grazed by a bullet or a foreign body of any kind, causing a hematoma or brush burn, or at least it corresponds to a brush burn, making a weak spot due to devitalization from the direct trauma or anoxemia from the thrombosed vessels or subsequent infection in a hematoma. This may

result in a perforation of the bowel, just as delayed rupture of the spleen occurs from incomplete tearing of the splenic capsule.

Local changes of course are dependent upon the cause of the wound. We may divide these into various headings which we have selected as causative factors:

1. Penetrating wounds by long pins or knives, daggers, or screw drivers produce a jagged wound which is straight in, as a rule, depending upon the angle at which it is introduced.

2. Perforating wounds vary with the distance and the velocity of the bullets or shrapnel. In bullets, the closer the gun is to the victim, the greater will be the damage. The wound of entrance is usually clean. The wound of exit is usually jagged. The wound of entrance may be stained with powder marks or burned if the gun is held close enough. The bullet as it leaves the barrel rotates on its long axis due to the rifles, particularly at its blunt end. It is this motion (movement of rotation) that keeps the point of the bullet toward the front. If a cylindroconoidal bullet were fired from a smooth bore, it would rotate on its short axis even at nine yards, thereby diminishing range and striking force but producing a bad wound. It revolves at a greater degree when it first leaves the barrel than after it gains momentum. Consequently, a bullet fired at close range will leave a very large wound of entrance and will actually tear an organ through which it passes (explosive effects). In fact, deep lacerations and bursting wounds occur in solid organs as a result of bullets fired at close range. At a distance and at a high velocity the wound of entrance and exit may be perfectly clean. Obviously the bullet which is soft and at a low velocity will produce a greater degree of damage than will a hard bullet at a very, very great velocity. Also, it is a well-known fact in ballistics that no matter how soft the bullet, velocity is the important thing. If the velocity is great enough, even a soft bullet will produce a comparatively clean wound. Even a straw may be driven through a solid tree trunk by the wind with great enough velocity. This is also true of bullets.

3. Blunt trauma usually produces a hematoma on the abdominal wall, or no mark at all, yet there may be a lacerated wound of the intestine. Usually this occurs on the mesenteric border and usually in the jejunum. However, we have seen lacerations in the colon and other parts of the intestinal tract.

4. Immersion blasts introduce laceration of the viscera, accompanied by hemorrhage. It is less likely to produce a tear in one of the larger vessels. Although the abdomen may be filled with blood, it will be from a tear in the walls or the solid viscera rather than from the vessel wall itself, as is the case in perforated wound.

5. Dehiscence of a wound or postoperative traumatic wounds correspond to eviscerations made by incised wounds by sharp instruments.

However, they occupy a special place in that they occur postoperatively and the pathology is somewhat different.

Dehiscence of a wound has been discussed previously. However, we are interested here in including it because it is in effect a postoperative laceration of the abdominal wall and injury to the viscera. The mechanism for this is a failure to secure healing and is due to one of the six factors which are known to delay repair (Chapter 3). As we have said previously, it is not so much the kind of suture material that is used, although there are extravagant claims for the various types, it is more dependent upon the general condition of the patient and the meticulous care with which the abdominal wall is closed. Such factors as abdominal distention, coughing, and intra-abdominal pressure play a role. However, in most instances the cause of the wound dehiscence will be found in the six factors which have been mentioned.

Recently, much has been written about the type of incision, early mobilization, and types of suture as causes for dehiscence. In our experience, early mobilization does not in any way predispose to dehiscence in a wound properly sutured, regardless of materials used, if the various layers of the abdominal wall are carefully approximated. It has been our practice to use nonabsorbable sutures. Following the dictum of Halsted, we do not believe that the suture material need be any stronger than the tissues being sutured. For that reason we have used silk, cotton, and linen. Silver wire, stainless steel, and tantalum wire may be just as good. We have also felt that a stay suture is not only unnecessary but is apt to strangulate tissues and interfere with blood supply. In that way it may be disadvantageous to use them. We are opposed to closing the abdomen with through-and-through sutures, preferring to close each layer carefully. The type of incision is definitely a factor.

A transverse incision has many advantages. A few may be listed here. (1) The blood supply of the abdominal wall is interfered with but little. (2) The nerve supply is not damaged. (3) The wound edges come together naturally. (4) If postoperative distension is present, it puts less strain on the wound than does a longitudinal incision. (5) The patient resists less during surgery and thereby affords better exposure. (6) The wound disruption is less frequent and is more easily repaired when it does occur. (7) The danger of postoperative hernia is less. (8) The patients may be allowed out of bed very early. However, there are disadvantages. They are not unique with this type of incision. We have found that the most important factor is the preservation of the transversalis fascia. The fascia may be incised parallel with its fibers and in this way the wound gains strength. One thing is sure concerning transverse incisions wherever they are made. They must be approximated accurately, and there must be no blood clot left in the wound to interfere with healing. Whatever the type of incision, if approximation is accurate and foreign bodies are avoided, union will occur, provided that the general condition of the patient

permits. All the surgeon can do is to adhere to sound surgical principles and try to improve the general condition of the patient by attention to those vital factors which he lacks such as water balance and blood volume. However, it should be said that the more nearly anatomical the incision, the better the healing. This is true not only of the abdomen, but elsewhere as well. Since the muscle-splitting incision adheres to the plane of the various layers, it is perhaps the strongest and it also has the advantages of having the suture lines in different directions.

Symptoms and Signs of Abdominal Injury

The symptoms and signs of abdominal injury are those of peritoneal irritation. These include (1) shock and (2) pain which may be moderated by shock, morphine, or stupor or confusion or intracranial injury. In civilian practice the symptoms may be confusing because of the frequent associated head, chest, and abdominal injuries. These have been discussed in Chapter 19 under Effects of Thoracic Injuries. However, in the patients who are not in profound shock, pain is an important symptom. Tenderness is variable and misleading due to superficial wounds. Rigidity is an important sign. However, even where there has been a thoracic wound with or without an abdominal wound, rigidity may be present. One of the most valuable signs is the presence of bowel sounds. In almost every instance of bowel perforation, there is an absence of bowel sounds. However, the absence of peristalsis is not a reliable indication that an abdominal viscus has been perforated because a silent abdomen frequently exists in connection with free blood in the peritoneum, retroperitoneal hematoma, severe contusion or blast injury, severe back injury, and severe thoracic injury. Therefore, it is a reliable sign when there is active peristalsis; it is not a reliable sign when there are no sounds present. In other words, we may say that when active peristalsis occurs, usually there is no perforation of a hollow viscus. Other factors in diagnosis are the careful history of the patient, if he can give it, a study of the urine, the anchorage of a Levine tube and study of stomach content, rectal examination and careful inspection of the examining digit to see whether there is free blood or not, proctoscopic and sigmoidoscopic examination, x-ray examination and this is important.

It may be assumed that all missiles maintain a straight course through soft tissues. Bony structures may divert the course. However, as a rule, if the wound of entrance and wound of exit have been established, the organs which may have been perforated may be carefully mapped out by the trajectory of that bullet. One important fact should be mentioned. The viscera may take a different position, depending upon the attitude of the patient's body at the time of the wounding. Particularly is this true with regard to the stomach and transverse colon which may hang down in the pelvis, and, therefore, a pelvic wound may actually cause perforation of the stomach. An x-ray film in the two planes will reconstruct very ac-

curately the track of the bullet, and this will enable the surgeon to anticipate the organ or organs which have been traversed. Rarely, a bullet takes a capricious course and may confuse the observer completely. Infrequently the bullet will lodge in a position that one may assume was caused by gravity after it came to a standstill.

Sometimes, in spite of the most careful observation, examination, and blood determinations, one is unable to make an accurate diagnosis. In such cases exploratory laparotomy is indicated. However, this should not be undertaken lightly. In civilian practice as a rule the questionable cases involve injuries to the head, thorax, and abdomen and they are caused by automobiles. It is no trick to make a diagnosis of surgical or nonsurgical abdomen in a penetrating wound, although this too at times becomes confusing, particularly high up in the chest, in which the bullet traverses the abdomen and diaphragm and may nick the cardiac end of the stomach or even the celiac axis, and low down in the buttocks, in which the pelvic viscera may be damaged. Even so, the chances of making a diagnosis is good, but in compound injuries of all kinds, including head, chest, and abdominal injuries, it is very difficult. This subject has been discussed in Chapter 19. Under such conditions, it becomes hazardous to do an exploratory laparotomy and, therefore, this should be reserved as a last resort. The highly questionable case many times requires a small incision in the abdomen done under local anesthesia to see whether or not free blood is present, and, if present, this would warrant exploratory laparotomy.

Summary.—A patient with an abdominal injury, no matter what the etiological factor may be, is first given resuscitative measures, particularly if in shock. While he is receiving blood or plasma or both, if conscious a careful history is taken and examination is made. This is routine and includes the general examination as well as the part which seems to be injured: the blood pressure, pulse rate, temperature, the abdomen carefully examined for rigidity, for masses, for tender area, auscultation to reveal the presence or absence of sounds, then a careful outline of the trajectory of the bullet, if it is a penetrating wound. Eviscerations of all kinds need very little examination except to determine the extent of the evisceration, and they require immediate action. Following this examination, the urine is examined; if the patient cannot void, a catheter is anchored and the urine is taken. Rectal examination is done to see whether or not there is any blood. If so, a proctoscopic examination can be done very quickly and sometimes is very informative. A scout film of the abdomen to determine the presence or absence of free air in the lateral decubitus position is very satisfactory. Shadows caused by the presence of blood may be mapped out by the roentgenologist.

Blood counts are done and plasma proteins and the hematocrit are determined by the copper sulfate method. These tests are a guide to therapy, but more important they help in the diagnosis of active hemorrhage. These tests are repeated at half-hour intervals if necessary.

It has been our observation that the higher leucocyte counts are indicative of liver and splenic injury. Leucocytes may reach 25 or 30,000 very quickly with the patient in shock and the temperature subnormal.

Having made the diagnosis, therapy is instituted as follows: A few general rules may be given concerning the treatment. (1) Arrest hemorrhage first, then treat the patient for shock. Operation may be necessary to stop bleeding. Therefore, when we say arrest hemorrhage first, we mean that resuscitation must be followed or accompanied by surgery. Therefore, while resuscitation is being affected, operation goes on. It is our practice to have two veins available for blood which may be used while the abdomen is being explored. In this way the blood volume may be restored as fast as it is lost. This is important because very frequently when the abdomen is opened a gush of blood ensues and the patient quickly bleeds to death unless a large volume of blood is available. We usually use an ankle vein and an arm vein, and we have our transfusion sets equipped with a bulb so that positive pressure may be used if necessary.

The incision should be simple and adequate. Since one does not know the exact location of the injury, the vertical incision is preferred to a transverse. The incision need not be restricted because plenty of room will be needed.

The plan of the operation may be briefly outlined as follows: Upon opening the abdomen, blood usually pours forth rapidly. Having mapped the course of the bullet, the surgeon is able to anticipate the possible blood vessels which have been severed or injured. Therefore, for example, in the upper abdomen, in a bullet wound from left to right, he would first look for an injury of the splenic pedicle, then the superior mesenteric perhaps, and so on. Higher, it might be the renal pedicle. In other words, he is prepared to arrest hemorrhage first insofar as possible. A major vessel cannot be identified without careful search in a pool of blood, which is difficult. Therefore, our practice is to have large perforated suction tubes available. The blood is mopped and sucked out and at the same time the surgeon will stop the bleeding with his fingers until he can clearly see its origin. Sometimes this is difficult because more than one vessel is bleeding at the same time. A clamp is placed upon the bleeding vessel until the whole area may be surveyed. Bleeding of very profuse nature means that a large artery has been torn. This must be seized and clamped before anything else is done. In fact, it is useless to attempt to survey the abdomen in a pool of blood, and it is equally dangerous to clamp blindly. The best clamp is the surgeon's fingers. Hemorrhage in the mesentery may give rise to a great amount of bleeding, and such bleeding requires careful control since the hemorrhage usually occurs from many small vessels. These vessels should be individually clamped and ligated. A transfixed ligature is good if the surgeon is able to see what he is doing. Mass ligatures are bad because they cut off blood supply which may impair adjacent loops of bowel and therefore should not be used.

Bleeding from the spleen cannot be stopped without ligating the pedicle of the spleen and that requires splenectomy. Bleeding from the liver may be arrested by pressure of gauze which may be poked into the rent temporarily until the abdomen may be surveyed. After the bleeding has been carefully controlled, the surgeon may turn his attention to inspection of the entire abdomen. Our plan is to find the holes in the intestine, remembering that if there is a hole of entrance, there is usually one of exit. This is particularly true of the stomach. Holes in the intestine cannot be felt and consequently the entire gastrointestinal tract must be stripped from the cardia down to the reflection of the peritoneum in the pelvis.

The surgeon uses a plan, starting in above and working his way down, and as he runs the bowel through his fingers, if an injury has been found or if a contusion has been found, it is repaired. Where one hole has been found, usually there are two and usually there are more. Simple suture is better than resection. If resection is done, however, single layer end-to-end anastomosis is better than side-to-side, because the patient's condition does not permit the more stable and stronger type of anastomosis. In general, drainage is not used. However, on the battle front, it is just exactly the other way. "Surgeons who drain most often save the most lives." In civilian life, however, it has been our rule not to drain unless there is a liver injury, and here only as a prophylatic measure to take care of the possibility of bile peritonitis. Under battle conditions, colon injuries certainly should be treated by exteriorization. In civil life this is not necessarily true, particularly if the injured person is seen within eight to ten hours after the accident. We routinely close wounds of the colon without exteriorization with good results. As a general rule, however, where a large tear has occurred within the colon, or if several tears are present, a proximal colostomy or appendicocecostomy is indicated. This is also true of the rectum. No matter how trivial the rectal injury, it probably will not heal unless a proximal colostomy is done and the hole in the rectum is repaired. This will be considered again later. Also, it is a fundamental maxim that in the extraperitoneal injuries, the retrorectal space should be drained through a posterior incision, anterior and lateral to the coccyx which may be removed to facilitate drainage.

The picture of shock may be produced by mere contamination of the peritoneum with a large amount of stomach or intestinal content. This implies a large hole in the bowel with peritoneal flooding. Shock may be produced also by associated chest and head injuries. It is our practice here to do an immediate plasma protein, hematocrit, and blood count and then replace the blood loss; then, in an hour or less, repeat the studies which will show us whether or not there is a continued hemorrhage or overwhelming infection of the peritoneum. The disturbance of the cardiorespiratory mechanism will be indicated by the symptoms and signs of anoxemia and circulation failure. The difference between continued hemorrhage and overwhelming infection of the peritoneum is apparent if

the patient is observed for an hour or two. In the latter case, there will be hemoconcentration with loss of plasma; in the former case, hemodilution with the loss of whole blood.

Treatment of Various Injured Organs in the Abdomen

The injuries to the various viscera of the abdomen will be considered under their respective headings. However, here we may consider general principles of handling specific injuries. **Penetrating and perforating wound of the bowel.** These must be carefully sutured. We usually employ an inner row of catgut and an outer row of silk sutures if the patient's condition will permit. If not, mattress sutures of silk are used of the Lembert type.

The suturing of a wound in the intestine is preferable to resection, but it must be ascertained that the lumen is adequate after suture so that obstruction will not occur. The blood supply to the segment of bowel should be carefully determined because a large hematoma from a rent in one of the mesenteric vessels may interfere with the blood supply and necessitate a resection. Injuries to the duodenum have been considered, and the importance of suturing wounds of the pancreas and biliary tract, stomach, and colon in connection with duodenal wounds should be emphasized. A word of caution should be sounded concerning so-called brush burns. The area may be small and seem superficial. However, later this may undergo a necrosis and a perforation may ensue. This is termed delayed perforation of the bowel. To avoid this, interrupted sutures of silk should be used. The devitalized area need not be exercised. Linear tears are closed transversely, but great distortion should be avoided because intestinal obstruction may occur and patients who have been severely wounded stand this complication poorly.

The Colon.—Exteriorization of the colon is necessary in war because of the large holes made in the colon by explosives and high velocity missiles and the time factor. In civilian practice the surgeon usually sees the patient early and may close the rent, although it is probably wise to do a proximal colostomy after such a closure has been effected. Exteriorization even in the Army was not practiced routinely for the right colon or the ileum. Here a repair was done or resection if necessary with an ileotransverse colostomy in an end-to-side fashion. If the patient's condition was poor, a Mikulicz type of exteriorization was done, making a spur four or five inches long. If this is done the dangers of secondary bowel obstruction are not so great; the spur permits crushing later and suturing by Mikulicz technique. In civilian practice, however, this is rarely necessary because the wound is usually not especially large or of such a nature that exteriorization is called for. Also, under battle conditions drains are used frequently. In civilian practice surgery usually is instituted before eight hours and drains are not used. This is especially true now with the aid of streptomycin, the sulfonamides, and

penicillin. Perforations of the sigmoid and the retrosigmoid and the rectum should be repaired, but proximal colostomy is practically always done under battle conditions. In civilian life, in injuries of the extraperitoneal portions of the large bowel, namely, the rectum, a proximal colostomy is done and the true nature of the injury ascertained. In other words, at the time of the colostomy, careful exploration is also done to determine whether or not there has been an injury to the bladder or to other viscera. After the damage has been repaired, the colostomy is completed and the patient is returned to his room. At the second stage, the extraperitoneal portion of the operation is done by suturing the rent in the rectum. This prevents fistulae from forming in the perineum. It should be said at this time, however, that not all observers are agreed that this rent in the rectum should be sutured. Some prefer to allow it to close itself after a proximal colostomy has been done. It has been our practice to suture this rent. A cecostomy is ineffective in defunctionalizing the large bowel. Therefore, a transverse colostomy, sigmoidostomy, is done. The fecal fistula which occurs through bone always requires excision. The other fistulae may heal but not those through bone. If there is an injury to the bladder, the same principles are observed; namely, the bladder is put at rest by diversion of the urinary flow and the opening in the bladder is closed. In civilian practice injuries to the rectum have been dealt with as colon injuries except that in addition to primary suture, a proximal colostomy is done to divert the fecal current until the wound heals. Also, we have used perineal drainage, but we have not found it necessary to resect the coccyx in order to institute it. Our reasons for closing the perforation of the extraperitoneal portion of the rectum are that although the colon is drained to prevent further contamination, yet a widespread infection may ensue in the retroperitoneal space and cost the patient's life. Furthermore, if the infection is controlled by chemotherapeutic agents, persistent fecal fistula may result which will require excision later on. For these reasons our custom has been to do a limited abdominal exploration and colostomy through a lower oblique incision; having found no injury within the abdomen, we next proceed to find the extraperitoneal wound. This is closed, the peritoneum covered over it, and a colostomy is done. The patient is then placed in the lithotomy position and the retrorectal space is drained. If the wound is directly in front of the coccyx, it may be necessary to do a coccygectomy at that time.

Wounds of the liver, no matter how they are produced, may be extremely dangerous. This is particularly true of the large comminuted lacerations of the liver that are ordinarily seen as a result of an automobile accident. Not only will the anterior portion of the liver be lacerated by the steering wheel, but due to fractured ribs the posterior portion of the liver also may be torn. There may be prodigious bleeding and the liver substance may be macerated. Such livers are difficult to suture and various methods have been adopted to control hemorrhage:

(1) Gauze packs will control bleeding, but when they are removed secondary hemorrhage may occur. (2) Skeletal muscle may be sutured into the liver tear. This works well in small wounds or surgical wounds made for biopsy. (3) The macerated wounds may be sutured by introducing a piece of omentum. We have used this method frequently. The omentum is placed into the rent and loosely sutured. This gives the stitches stability. The omentum may be laid over the torn area kept in contact by gauze packs. However, this predisposes to infection and when the pack is removed there may be secondary hemorrhage. (4) More recently the use of cellulose acetate gauze which is absorbable has been made available and works very well. This gauze which is sutured directly into the wound is absorbed. Suturing is really unnecessary in many cases when this gauze is employed. However, where large vessels are involved, it is risky. These should be tied and the gauze sewed in place. (5) *Through-and-through* sutures using a large blunt needle and taking large bites is useful if there is not too much contusion. Perhaps the most important point to make in regard to injuries to the liver is adequate drainage of the subphrenic space and Morrison's pouch. The reason for this is that all liver damage of any proportion causes a considerable leakage and may produce a bile peritonitis. We have frequently closed up the abdomen without drainage in civilian practice where the injury has been modest and the tear adequately sutured and where the lesion has been repaired within the first eight hours.

Injuries to the spleen usually require splenectomy. Sutures in the spleen are unsatisfactory and secondary hemorrhage may occur. Therefore, splenectomy is the treatment of choice.

Injuries to the kidney require nephrectomy. However, small wounds of the kidney may be treated conservatively and may be sutured. If the major blood supply is injured or if an injury is near the hilus, usually the kidney must be removed. Injuries to the ureter are closed by sutures. In battle areas, the ureter was usually injured so extensively that the primary repair was very difficult and nephrectomy was the procedure of choice. In civilian practice, however, where adequate facilities are usually available, primary suture or excision and anastomosis are attempted.

Wounds of the great vessels have been discussed in Chapter 17, and thoracoabdominal lesions have been adequately reviewed in Chapter 19. Other injuries which may occur within the abdomen such as the gall bladder and the pancreas, require special consideration.

The **gall bladder** may usually be saved by draining it. The **pancreas** should be sutured and a drain should be placed through the gastrohepatic or gastrocolic ligaments.

Treatment of **intra-abdominal injuries due to blunt trauma** will be discussed under injuries of small intestines. However, it may be said at this time that in severe abdominal contusions, especially in children with all the symptoms and signs of peritoneal irritation, together with

shoulder pain, an injury to the bowel should be suspected and primary suture should be done. If seen within eight hours, drainage is unnecessary.

Postoperative dehiscence is a form of injury which results in an evisceration and must be treated promptly. The treatment of postoperative separation, if it is complete, requires, first of all, recognition, and this is usually evident by the fact that in a normal wound there should be no perceptive amount of drainage. Dressings are not usually disturbed for eight days unless there is pain, fever, or appreciable exudate. In the latter case one should always suspect dehiscence, particularly if serous or if accompanied by vomiting and by signs of shock. Although some have advocated the use of adhesive to hold the skin edges together, particularly in bedridden patients, it has been our experience that where dehiscence has occurred the best method is to resuture the wound immediately. This is a life-saving measure. Our plan is to start transfusions immediately and to introduce a Levine or Miller-Abbott tube to empty the bowel of gas as much as possible. Under local anesthesia, the wound edges together with all the layers of the abdominal wall, are brought together by through-and-through sutures. We have used heavy silk or silkworm gut, although some have preferred through-and-through sutures of silver or other wire. It is rarely possible to suture the abdominal wall in layers because of their friability. In addition, hematomas have formed and infection is present. The time consumed in separating and identifying the layers would be more than the patient could stand. After cleansing the skin margins with physiological saline in large quantities, the eviscerated organs are washed with the same solution and replaced. If necessary, a little Pentothal sodium may be used intravenously. The through-and-through sutures are introduced, *and in addition the skin is closed by interrupted silk* sutures. In bad-risk patients, until blood transfusion has been done and the bowel has been emptied of its gas, adhesive strips may be passed from side to side and the wound edges held together. It is surprising under such conditions that very frequently the wounds will heal, and we have observed very few instances of postoperative hernia. It should be emphasized that the local conditions which caused the breakdown be rectified insofar as possible. This will usually be the presence of a small portion of extruded omentum. Obviously the general condition of the patient should be improved by attention to water balance and blood volume. Vitamins should be given, particularly vitamin C.

The immersion blast injuries are treated by immediate exploration and all rents sewed promptly and bleeding controlled. The entrance of water into the rectum may produce a very long jagged rent in the colon. This is dealt with under battle condition by exteriorization. In civil life occasionally an air hose is introduced into the rectum as a prank. This may produce a tear in the colon requiring laparotomy and suture of the torn bowel or its exteriorization if too badly torn. There is much bleeding in the coats of the bowel wall so that approximation *of the layers*

may be difficult and insecure. Three plans are available. (1) The devitalized area if limited may be excised. (2) Resection may be done or the colon may be exteriorized. (3) A proximal colostomy is indicated if there is any doubt about the suture line. Rarely, the colon may be injured by the introduction of a glass bottle or stick in the rectum in sexual perverts, causing a tear. This requires immediate operation and suture of the rent. The postoperative care of all abdominal wounds includes attention to water balance and blood volume; also the prevention of distention by the use of the Levine tube with suction. The use of chemotherapeutic agents and antibiotics help. Streptomycin will help in the control of colon bacillus infection and its prevention. Penicillin and sulfadiazine help in the control of streptococcal and staphlococcal infections.

In **combined thoracoabdominal injuries,** oxygen is used postoperatively. Also, it should be added that very frequently an abdominal injury is accompanied by a diaphragmatic tear or laceration. This should be repaired so that pneumothorax, empyema, and diaphragmatic hernia may be avoided.

A consideration of injuries to the abdominal wall must include the subject of **external fecal fistula.** Although they have a variety of causes and they are not, strictly speaking, an abdominal wall pathological entity, yet they are a group which may be properly considered at this time. The law of fistula as given in Chapter 5 states that if the normal channel is open, the artificial channel will close with the following exceptions: (1) fistulous tract lined with mucous membrane, continuous with the skin; (2) tuberculous fistulae; (3) mycotic fistula; (4) new growth; (5) foreign bodies.

Fistulae may be internal as well as external, or there may be an internal opening in addition to the one on the outside. The term fecal fistula is not entirely proper because it includes drainage from the intestinal canal whether it is fecal or not, such as duodenal content. Also, there may be biliary or urinary fistulae. If possible, the organ from which the tract originates should be used, such as gastric, duodenal, cecal, urinary vesical, gall bladder fistulae, etc. Nor is it proper that we speak of them as abdominal since some of them occur in the sacral, lumbar, or even in the thoracic region, depending upon their cause and their situation. Most fistulae do occur in the colon or ileum because of the lesions which occur in these parts.

The treatment of fistula depends upon its cause and its duration. Therefore, it is important that the cause be determined if possible. In a penetrating wound or a perforating wound or a stab wound, the fistula is established by the injury and is closed immediately. However, if it is not seen within forty-eight to seventy-two hours, it is perhaps best to wait and close it later. This also applies to fistulae which occur postoperatively. The reasons for postponing the closure of such fistulae is, first of

all, to permit local immunity to become established. Following the injury there is much inflammation in the bowel wall and peritoneal cavity. Repair at this time might spread the infection. If other conditions do not warrant immediate surgery, it is perhaps best to let the fistula remain as a safeguard against obstruction and later go in and close it. Another reason for waiting following wounds is that many of these fistulae will close spontaneously. Most wounds are made within organs which are not previously diseased. A normal channel is open and chances are that the fistula will close.

Postoperatively and as a result of disease it is a good idea to attempt to establish the cause. However, in many cases, this is difficult. In addition to traumatic wounds which may cause a fistula, many other causes should be be mentioned at this time.

Etiology of persistent fistula: Persistent fistula may be caused by the following: (1) Inflammatory lesions of the bowel. In this group are included diverticulitis, regional enteritis, ulcerative colitis, and appendicitis. Also in this group are the specific types of infection; namely, tuberculous enteritis and actinomycosis. (2) Inflammations outside the bowel; namely, pelvic inflammatory disease, tuberculosis of the abdominal cavity or tuberculous abscess, retained foreign bodies, osteomyelitis. (3) New growths which ulcerate and perforate, producing a persistent fecal fistula. (4) Obstructions from various causes with spontaneous or surgical establishment of a fistula, thereby relieving the obstruction. This fistula will remain open. (5) Postoperative fistula may occur without any apparent cause. It is assumed that in most cases some injury or severe infection was present at the time of operation and a foreign body was left in the abdomen or that the bowel was traumatized and not recognized so that repair was not done, thereby causing a fistula. Sometimes the cause of fistula cannot be determined, even after careful microscopic examination.

Diagnosis as to the Type of Fistula.—The history of the cause is important; trauma, operation, purposeful fistula are all obvious. The diagnosis as to the cause may also be ascertained by taking a biopsy and studying the fistulous tract. Not infrequently the surgeon will discover actinomycosis or tuberculosis or even carcinoma. If no specific cause can be found, careful examination by x-ray with Lipiodol injected into the tract or barium meal or enema to determine the presence of an obstruction should be done. This method may also provide valuable information concerning the course and communications of the fistula and, above all, the patency of the normal channel.

The Treatment of Fistula.—If the normal channel is open and the fistula remains, then the cause of the fistula must be sought because the treatment will depend on the cause. The treatment may be divided into the preoperative preparation and the surgical procedure and will vary according to the pathology that is determined. All patients with bowel fistula are fed a nutritious diet and attention is given to the water balance

and blood volume. In addition, succinylsulfathiazole, 1/4 Gm. per pound of body weight, is given by mouth and an equal amount is injected into the distal portions of the bowel. Sulfathaladine may be used in smaller doses, approximately 1/10 Gm. per pound of body weight. If the fistula tract is short and if found to contain only mucous membrane which has grown to the skin, a conservative operation may be done which consists of curettement of the fistula tract. This may result in a cure. Sometimes this may be accomplished by use of silver nitrate which is not as reliable or successful. The second most common method of dealing with fistula is excision. This is done by making a semilunar incision around the opening and sewing the skin over the fistula so that the bowel wall is turned in. This is done in the so-called aseptic manner. However, with the advent of *antibiotics and chemotherapeutic agents, the bowel wall is freed and turned* in, in a surgical manner and the abdomen closed without drainage. In compound fistulae it is necessary to do a preliminary colostomy or enterostomy, or a short circuit may be made around the fistulae. This may be a definitive procedure or it may be a first stage. As a rule it is the latter. For example, a fistula of the ileocecal region may be temporarily interrupted by dividing the ileum and doing a transverse colostomy. The second stage consists of removing the entire area just as in carcinoma. In fact, neoplasia may be the cause of the fistula and may warrant wide excision. If the short circuit is to be temporary, the ileum is not divided and a lateral anastomosis is made between the ileum and transverse colon. At a later date this may be rectified after the fistula has been closed or it may be left in situ. This procedure is frequently done in regional enteritis. In fistulae due to severe chronic ulcerative colitis, ileostomy may be done as a definitive operation, as a preliminary stage to colectomy. We have many cases of ulcerative colitis with fistulae which have closed after the ileostomy and no further surgery was necessary. For fistulae of the sigmoid, a transverse colostomy may be necessary to improve the patient's condition and to give the fistula a chance to close spontaneously. More important, these side-tracking operations permit the patient's condition to improve and allow the local inflammatory reaction to subside. Simple fistulae may be excised by elliptical incisions, closure of the fistula, and then resection. Usually, however, it is better to make an adequate incision where the cause of the fistula is not known for the purpose of exploration. After careful preparation, this may be done with safety, and the fistula itself is not removed until the cause of it is ascertained. In seriously ill patients, the side-tracking operation will have been done, and the fistulous *opening may be carefully dissected* out and a resection of all diseased tissue, even that which is remotely diseased, may be accomplished so that primary union may occur. In case of carcinoma, wide excision is necessary, not only around the fistula, which may contain malignant cells, but of the involved bowel as well. The wound where the fistula was excised should be closed very loosely so that abdominal wall infection will not ensue.

The plan of removal of the fistula should be by adequate exposure and sharp dissection because the bowel that becomes attached to the fistula is very friable, and in separating the loops they may be torn. Fistulae which pass through bone, as has been said, will not close unless they are excised. They are particularly hard to heal. These are seen in the region of the buttocks following gunshot wound which has penetrated the rectum or colon.

In summary, the treatment of fistula reverts back to the cause, and the law of fistula will hold in fecal fistulae as elsewhere. The postoperative care of the patients with fecal fistulae is the same as those treated with bowel resection. They should be given large doses of penicillin and sulfonamides and streptomycin as indicated. Nothing is given by mouth; a Levine tube is passed with Wangensteen suction. Fluid balance and blood volume balance is maintained. These patients usually do very well and the percentage of recovery is high.

Inflammation of the Anterior Abdominal Wall

In the newborn, inflammation of the anterior abdominal wall is seen as an *omphalitis.* Although this condition now is extremely uncommon, it is encountered often enough to warrant some description. The umbilical vein pierces the abdominal wall and continues inward at the inferior edge of the falciform ligament, communicating with the portal system and also with the inferior vena cava by the way of the ductus venosus. After birth the ductus venosus becomes obliterated and forms the ligamentum venosus, and the anterior portion of the umbilical vein becomes obliterated and forms the ligamentum teres. The two umbilical arteries pass through the abdominal wall and then course downward. They become the hypogastric vessels between the transversalis fascia and peritoneum and join the internal ileac arteries. Soon they become obliterated also, and as we shall see they form the obliterated hypogastric artery bounding a space through which a direct hernia may find its way. These venous and arterial channels may remain open and, if they do, infection may find its way upward because of thrombophlebitis or downward through an infected arterial embolus. Furthermore, the lymphatic drainage as we have seen is prodigious, permitting infection to spread along the lymphatics downward and upward into the inguinal and axillary regions, respectively. Last, the infection may spread by direct extension into the abdominal cavity.

Omphalitis is caused by infection of the umbilical cord stump. As in gangrenous stomatitis and other severe infections, "it takes two to make a bargain." Namely, "it is the soil rather than the seed" which is at fault. The organism most frequently encountered is the hemolytic streptococcus; next, the *staphylococcus aureus.* Rarely the colon bacillus is at fault, although, theoretically at any rate, the colon bacillus is not found in the gastrointestinal tract until eight to ten hours after birth.

The pathology is as follows: Granulation tissue seems to persist in the umbilical stump and there is a preumbilical cellulitis that seems to

spread. This occurs within the first few weeks of life. The redness and the induration is extensive, and soon the entire preumbilical area is involved. The infection may follow one of several courses: (1) The infection may remain local and form an abscess. This may break and the entire process may undergo resolution. (2) Resolution without abscess formation may occur. (3) Necrosis and sloughing may result. (4) Necrosis with absorption may be the reaction. (5) There may be blood stream invasion with severe septicemia and septic pylephlebitis, involving the portal vein, and a multiple abscess of the liver. (6) The infection may spread by direct extension into the peritoneum, causing peritonitis. The cases which we have seen have included all of these types. Most cases of omphalitis will subside under treatment of large doses of penicillin, 50,000 units given intramuscularly every three hours. Locally, protection of the inflammatory lesion with penicillin ointment has been our treatment of choice. Local types of infection have been encountered, but rarely. Usually the blister will break without surgical intervention. *Cellulitis* with involvement of fascial planes is very serious and may cause a great deal of sloughing. This type of reaction is seen in babies who are malnourished and in poor physical condition; also in children who have had scarlet fever or measles or other infectious diseases in early life. In these cases with extensive undermining, the skin must be excised overlying the necrotic tissue, and after granulation forms, skin grafting in stages is pursued. Severe bacteriemia or septicopyemia may result in metastatic abscesses. These may be seen in the fingers and legs. If a septic pylephlebitis occurs, there may be jaundice with multiple abscess of the liver. In those cases which spread to the peritoneal cavity, the mortality rate is extremely high. Peritonitis starts very rapidly. However, here again, with the use of penicillin, streptomycin, the sulfonamides, and peritonitis regimen, the results have been better.

Omphalitis in older children occurs not infrequently. This may be due to the fact that the umbilicus is perhaps the filthiest part of the body and in many children rarely, if ever, is washed. Furthermore, children have a habit of introducing foreign bodies in the umbilicus, such as small pieces of gravel, sand, or toys, setting up an inflammatory reaction. Often the first sign of an omphalitis consists of swollen inguinal nodes. These lesions heal very readily after the causative foreign body is removed and the navel washed with soap and water.

Other infections of the anterior abdominal wall occur under the following circumstances: (1) Injuries. (2) Postoperatively. (3) As a result of visceral infections.

Injuries of the abdominal wall have already been discussed. The infections which follow such injuries are usually complicated by an injury to the colon or intestinal tract. Very rarely a superficial injury becomes infected. However, in most instances this is due to the presence of a foreign body and follows the rule of skin infections as discussed in Chapter 16.

The treatment of injuries to the abdominal wall is the same as injuries elsewhere on the body. However, it must be borne in mind that injuries on the abdominal wall, although merely contusions, may be accompanied by injury within the abdomen.

Postoperative infections of the abdominal wall have been discussed under Clinical Types of Suppurative Inflammation, Chapter 5. Here we discussed stitch abscess caused by the *Staphylococcus albus* and *aureus*, the colon bacillus infections, and also the symbiotic infections which occur in badly debilitated individuals, following operations and particularly following colostomy or enterostomy. Infections of the abdominal wall which follow visceral infections usually occur after the viscus has become attached to the parietal peritoneal surface; then by erosion and secondary infection, the abdominal wall is involved. Sometimes an abscess will point over the gall bladder area following perforation of a gangrenous gall bladder. This is also seen in perinephric abscess which points in the loin, or for perforating carcinoma with abscess formation, appendicitis, and diverticulitis with abscess. The abscess may be recognized and drained surgically, at which time its origin may be ascertained, or later, after careful study by x-ray and the injection of Lipiodol through the sinus tract.

Rarer causes of infection of the abdominal wall include *cellulitis due to extravasation of urine* from the male urethra below the triangular ligament which spreads through the subcutaneous tissue of the external genitalia and directed by fascial attachments to the pubic arch and inguinal ligaments, sometimes passing up into the abdominal wall.

Another rare form is cellulitis of the properitoneal fat. This may be associated with perinephric abscess or a perivesical abscess through an infection in the properitoneal fat posteriorly from retroperitoneal hematoma following the injury. Cellulitis of the abdominal wall is more likely to occur from a kidney or colon lesion than any other source.

Of the specific types of infection of the abdominal wall, we must include tuberculosis, actinomycosis, and, last, a carcinoma of any variety is apt to cause infection due to the formation of fistulae.

Abdominal Incision

The diagrams will show the various types of abdominal incisions which have also been discussed in Chapter 3, Figs. 4-7. The principles involved in wound healing must be scrupulously observed in abdominal incision. The so-called anatomical types offer much in facilitating wound healing and in the prevention of dehiscence.

Neoplasms of the Anterior Abdominal Wall

Neoplasms of the anterior abdominal wall may be divided into benign and malignant tumors. The latter may be subdivided into primary malignant tumors which may be carcinoma, sarcoma, or melanoma, and a second subdivision of the malignant group include metastatic malignant

neoplasms which may be implantation cancer, malignant lymphomas, and metastatic growths from intra-abdominal organs. The last group includes a group of miscellaneous lesions which simulate tumors in the anterior abdominal wall.

Group 1. Benign tumors of the anterior abdominal wall. This group consists of many varieties including lipoma, neuronevus, hemangioma, epithelial papilloma, fibroma, neurofibroma, teratoma or teratotic papilloma, desmoid tumors, lymphangioma, dermatomyoma, Schwannoma, and lymph gland adenoma. Some of these lesions have been considered in other chapters, particularly Chapters 15, 16, and 17. A few of this group deserve special attention.

The neurogenic group of neoplasms all demand careful surgical eradication. This is true of others of the benign group such as the lipomas, the neuronevi, the hemangiomas, epithelial papillomas, the fibromas, neurofibromas, the teratomas, and teratotic papillomas. Lipomas are by far the most common of all tumors seen in the abdominal wall. The nevus unius lateralis or neuropathic papilloma demands wide excision because it may undergo malignant degeneration or transformation. This is true also of the neurofibromas. Neurofibromas may be located within the abdominal wall or within the abdominal cavity. The vascular group of benign neoplasms, if very superficial, may be treated with carbon dioxide snow, but if they are elevated, they should be excised and a skin graft placed over the excised area or a skin flap should be cut.

Lymphangiomas are best treated by excision in stages if they are extremely large. Desmoids constitute a very interesting, though rare, entity. They occur in children as well as adults and are seen as hard fibromas in the flat muscles of the anterior abdominal wall. They are more common in young women, although we have seen some desmoids in young males. The tumor has been described as an unincapsulated infiltrating fibroma of fascial or aponeurotic origin. Its microscopic appearance varies from that of a cellular fibroma to that of a low-grade cellular fibrosarcoma. These growths are said to occur in skeletal muscle elsewhere, but they are extremely rare. It is a characteristic finding that when one encounters a desmoid, one is apt to make the mistake of calling it a fibrosarcoma. The cause, of course, is unknown. Most of these growths occur in young parous women; therefore pregnancy has been said to be of etiological significance. Since the growth does occur in young males, this certainly could not be the only predisposing factor if it has a bearing at all. It is perhaps more correct to assume that during pregnancy tension on the fascia and the aponeurotic fibers may play a role. Desmoids are dense, hard, and fibrous, and although they may be fairly circumscribed, more often a definite capsule cannot be found. They are usually solitary. When these tumors are found elsewhere in the striated muscle, they have a tendency to infiltrate into the joints and become adherent to bone. The desmoid tumors having their origin in the

posterior sheath of the rectus may become firmly attached to the parietal peritoneum. They rarely involve the skin, although cases have been reported where the skin ulcerates. They are not vascular, yet they do not undergo necrosis or liquefaction. The microscopic appearance is that of a fibroma plus bundles of striated muscle fibers in various stages of atrophy. Desmoid may be confused with neurofibroma or a neurofibrosarcoma. Some pathologists think that a desmoid tumor is really a perineural fibroblastoma, and some specimens suggest this origin, but there is no proof of this.

The treatment is complete surgical excision, and this must be wide and radical because there is a great tendency for local recurrence. In most cases the patient should be warned against subsequent pregnancy because of the high rate of recurrence following childbirth. Strangely enough, the desmoid does respond to x-ray therapy, particularly in the female. This is thought to be due to the effect of the therapy on the ovary which stops the production of ovarian hormones. It is more resistant to radiation in the male. However, following radiation castration in the male, it undergoes regression. Since the growth does not metastasize to regional lymph nodes, the prognosis is extremely good if local extirpation is complete.

Malignant tumors of the anterior abdominal wall include carcinoma of the epidermoid and basal-cell type and adenocarcinoma; also sarcoma which may be neurogenic, spindle-cell, rhabdomyosarcoma, dermatosarcoma, liposarcoma, and granulation tissue sarcoma, and the melanomas; melanocarcinoma of the skin is common, yet in the anterior abdominal wall it is relatively rare.

Chronic irritation such as that seen in burn ulcers of the lower extremities may produce carcinoma (Marjolin's ulcer), and kangri burn cancers of the Japanese are examples of epidermoid cancer brought about by repeated application of heat. An earthenware bowl heated by wood charcoal is worn under a single loose garment by the poorer class of Kashmir. The habit of wearing a portable oven against the abdominal wall for the maintenance of body heat is also prevalent in Japan. Carcinomas of the abdominal wall in America are extremely rare except following radiation dermatitis. Rarely sebaceous and sweat gland adenoma may be precursors to adenocarcinoma.

Primary carcinoma of the anterior abdominal wall metastasizes slowly. Complete extirpation by surgical means followed by radium or low or intermediate voltage x-ray gives good results. Cancer which arises postoperatively and results in chronic draining sinuses or fistulae offers the most serious prognosis. In this way it resembles the marginal ulcer resulting from a burn in the lower extremities. *Granulation tissue sarcoma*, according to Ewing, is a process arising from lacerated chronically infected wounds or in reactive organization of hematomas. These must be thoroughly excised. *Malignant melanomas* are even more malignant when they occur on the anterior abdominal wall than elsewhere.

This is due to the fact that both lymphatic and venous components are involved, and since the abdominal wall is well fortified with lymphatic and blood vessels, metastasis is early. The growths, together with all *related lymph nodes that may become involved, should be removed.* X-ray and radium have little effect.

Metastatic malignant tumors of the anterior abdominal wall are fairly common. They may arise from carcinoma of the ovary, stomach, uterus, lung, kidney, breast, sigmoid, cecum, rectum, liver, pancreas, gall bladder, vulva, and undetermined sources. In Chapter 15 we discussed the possibility of implantation cancer, and this was particularly true in exteriorizing operations for carcinoma. We have also seen it following excision of carcinoma of the breast with skin-grafting implantation.

The *metastatic sarcomas include melanoma*, teratoma of the testis, mesodermal mixed tumor of the vulva, and liposarcoma. Endothelioma and multiple myeloma rarely involve the abdominal wall secondarily. The treatment for secondary carcinoma or metastatic carcinoma and metastatic sarcoma is purely palliative since the origin of the growth is evidently still present or has not been completely removed. However, in implantation carcinoma or in direct extension of carcinoma from an abdominal organ, a wide excision of the abdominal wall, together with the primary growth, may prolong life and occasionally result in a cure. We have seen one such case of carcinoma of the cecum in which the abdominal wall was involved. A radical operation included the terminal ileum, cecum, ascending colon, half the transverse colon; and the right lower quadrant of the abdominal wall, where a fistula had established itself, was excised and flaps were swung over it to close the abdominal defect. This resulted in temporary arrestment of the disease and the patient survived for over four years.

Malignant lymphomas occur in the anterior abdominal wall. These include lymphosarcoma, Hodgkin's disease, leucemia, and, rarely, mycosis fungoides.

The last group consists of miscellaneous lesions which simulate neoplasms of the abdominal wall. In this group may be included the chronic inflammations and cysts including sebaceous cysts, urachocysts, sweat cysts, radiation ulcer, fat necrosis, pyogenic granuloma, tuberculosis, actinomycosis, and spontaneous hematoma. Tuberculosis has been encountered only rarely. Endometriosis involving an abdominal scar following a cesarean section and also in the umbilicus is occasionally seen. Spontaneous hematoma was formerly seen fairly often in typhoid fever but is a comparatively rare lesion now. Of all these lesions, perhaps those which resemble carcinoma most are the radiation ulcers, fat necrosis, and tuberculosis.

Diagnosis can be made only by biopsy. An apparent abscess should be drained, but a biopsy should be taken from its wall. The same is true of sinuses and fistulae. Tumors of the abdominal wall, therefore, may be

primary or secondary. In any event they should not be neglected. They should be removed for biopsy, if for no other reason. Very often a supposedly benign tumor gives a clue to an intra-abdominal lesion which is malignant.

PERITONEUM

Embryology

We have already discussed the development of the somatopleure and the splanchnopleure. It will be recalled that in the very early embryo the mesoderm splits laterally in two layers, the dorsal known as the somatic and the ventral known as the splanchnic mesoderm. These layers persist in the adult, the somatic mesoderm giving rise to the pericardium, to the parietal pleura, and to the peritoneum, while the splanchnic layer forms the epicardium and the myocardium, the visceral pleura of the lung, the mesenteries, and the mesodermal layer of the gut. The somatic mesoderm and the ectoderm with the tissues that develop between them constitute the body wall. This is called the somatopleure. Also the splanchnic mesoderm and the enterderm with the mesenchymal tissue between them constitute the wall of the gut and this is termed the splanchnopleure.

The cavity between the somatopleure and the splanchnopleure is the coelom or the body cavity. Later the coelom is divided into the pericardial cavity, pleural cavity, and the peritoneal cavity as has been previously discussed. The somatic and splanchnic layers of the mesoderm form on their coelomic surfaces a single layer of squamous cells called the mesothelium. This is the covering layer of the pericardium, pleura, peritoneum, mesenteries, serous layer of the viscera, and lining of the tunica vaginalis in the scrotom. From this mesothelium, according to Prentiss, is derived also the epithelium of the genital glands and the ovarian ducts.

Great variations occur in the development of the peritoneum and the mesenteries within it. For example, the various hollow viscera may be normally placed and unattached, or they may be abnormally placed and attached to an abnormal mesentery. For example, the cecum may be attached to the mesentery of the small bowel; that is, the ileomesentery. Sometimes the mesentery is extremely short or long, permitting great variation in the mobility of an organ or of the hollow viscera. The greater omentum normally arises from the stomach and later overlies the transverse colon to which it becomes fused. Sometimes with incomplete rotation of the colon the stomach and colon are not connected with each other by the gastrocolic ligament and the greater omentum hangs only from the colon.

Again various membranes have been described, some of which are more or less common. These were formerly thought to be of importance in intestinal stasis, particularly in the lower ileum, known as Lane's band. A congenital band or membrane may be differentiated from one which forms as a result of inflammation. The con congenital band usually has its vascular supply in lunettes just as is found in the mesentery. The membrane or band of new formation will have parallel lines of vessels so that as the membrane stretches, these may lose their lumen and become obliterated, thereby permitting the membrane to be absorbed. This is not uniformly true. However, as a rule, it is very evident. There is also a congenital membrane often associated with incomplete rotation of the cecum. The cecum may come to lie across the third part of the duodenum and may obstruct the duodenum by its pressure, and the cecum is attached to the upper lateral abdominal wall by an abnormal band. This band of peritoneum is divided and the duodenal obstruction is released by permitting the cecmum to assume a position on the left side of the abdomen.

Other types of congenital anomalies of the peritoneum include internal herniae which have been discussed previously in the chapter; also persistent fetal structures, including persistence of the omphalomesenteric ducts or arteries, persistence of the

urachus, persistence of the umbilical vessels or the urachal vessels. The anomalies of blood vessels are important because of the possibilities of development of intestinal obstruction. In the young embryo the yolk sac is nourished by a network of blood vessels. These soon converge to form two omphalomesenteric arteries and two omphalomesenteric veins. The left omphalomesenteric artery disappears, but the right persists and accompanies the duct in the umbilical cord. This also disappears before birth, except on its mesenteric portion where it ultimately becomes the superior mesenteric artery. The two omphalomesenteric veins disappear before birth except the proximal end of one which becomes the portal vein. The umbilical vessels appear early in the embryo, first as endothelial spaces in the mesenchyma in the body stalk. There are two arteries and two veins which run from the placenta to the embryo to convey blood to and from the fetus. The two arteries persist until birth when they become the obliterated branches of the hypogastric arteries which are important in delineating the inner portion of Hesselbach triangle. One of the veins disappears very early, but the other functions until birth as the umbilical vein, which then becomes the ligamentum teres or the falciform ligament. The urachial artery is a small vessel which arises from the superior vesicle branch of the left hypogastric artery. It courses along the anterior aspect of the urachus and into the cord supplying the allantois. At birth this artery is obliterated and becomes a small fibrous cord in close proximity with the urachus. At operation this cord is frequently encountered.

The peritoneum in the male forms a closed sac (in the female there is a communication to the exterior through the Fallopian tubes). The peritoneum is a continuous layer of serous membrane which is, so to speak, indented by the hollow and solid viscera of the abdomen, to which it is closely attached (the visceral peritoneum). Where these indentations occur there are closely approximated folds which form the mesentery of the small intestine and of part of the colon. The unusually long fold turning back on itself and hanging from the stomach and transverse colon is the greater omentum, and, with these organs, the hepatogastric ligament, and the transverse mesocolon, bounds the lesser peritoneal space. Between the indented parts (the visceral peritoneum) and the free part (the parietal peritoneum) is the general peritoneal cavity. The lesser and general acs are connected through the gastroepiploic foramen (foramen of Winslow). Heavy folds on the peritoneum are also attached to solid organs, forming their ligaments.

Like other mesothelial tissues (pleura, pericardium, synovial membrane), the peritoneum is composed of a thin layer of fibrous tissue covered with endothelial cells (the tunica serosa). A layer of areolar tissue (the tela subserosa) connects the peritoneum with the underlying fascia or viscera. This latter layer varies in amount in different locations, being plentiful under the parietal portion and almost entirely absent on the visceral portion covering the bowel. Normally the membrane secretes only sufficient fluid to lubricate its surface. Except for this small amount of fluid, the sac is empty and its walls lie in contact with each other.

Subdivision of the Peritoneal Cavity

From the surgical point of view, the peritoneal cavity may be divided into four great subdivisions: (1) supracolic, (2) right infracolic, (3) left infracolic, (4) pelvic. All of these subdivisions communicate freely with one another behind the anterior abdominal wall as well as on each side along the paracolic gutters. These gutters are important for the ascent or descent of an exudate which readily makes its way from the upper part of the abdomen along the lumbar region into the iliac regions and thence into the pelvis. Pus from the pelvis or a perforated appendicitis or diverticulitis may ascend along these gutters, reaching the supracolic space.

The supracolic space (phrenocolic) is bounded below by the transverse colon and the transverse mesocolon, above by the diaphragm and laterally by the lateral abdominal wall, anteriorly by the anterior abdominal wall, and posteriorly by the posterior ab-

dominal wall. The supracolic compartment is divided into a right and left portion by the falciform ligament. Within this compartment lie the subphrenic spaces, right and left. These are potential spaces which lie between the liver and the diaphragm on each side of the falciform ligament of the liver. In liver abscess, gall bladder disease, perforation from peptic ulcer, appendicitis, and intestinal injury, collections of pus or exudate may accumulate here, forming a subphrenic or subdiaphragmatic abscess. Suppuration in the right half of the phrenocolic space is generally secondary to leakage from an ulcer of the first part of the duodenum or disease of the gall bladder or bile duct, while the left half of the space is more usually infected from perforation in the stomach.

"*If the general peritoneal cavity is compared to a bag, the bursa mentalis* (or lesser cavity) might be represented as a pocket lying behind the opening into it by a narrow orifice—the foramen epiploicum." (Cunningham.) The omental bursa may be looked upon as a pocket or a diverticulum of the supracolic division of the peritoneal cavity.

The lesser peritoneal space lies behind the stomach, which, with the gastrocolic ligament, forms its anterior boundary. On the right side, it is bounded by the hepatoduodenal ligament, which closes the space between the liver and duodenum. A small opening in this ligament, known as the gastroepiploic foramen (foramen of Winslow), connects the lesser with the greater peritoneal cavities. This *foramen* is important to the surgeon because by putting his finger in it he may palpate the common bile duct, which lies behind it, *with the hepatic artery and protal vein. Below*, the cavity is limited by the transverse colon, on the left by the spleen and lienorenal ligament, and behind by the posterior abdominal wall. Within this cavity is the pancreas. Should the gastroepiploic foramen become sealed by exudate when there is pancreatic disease or posterior gastric perforations, a large collection of fluid would (and frequently does) accumulate.

By adhesions of the transverse colon and the greater omentum to the anterior abdominal wall, this supracolic subdivision of the peritoneal cavity may become more or less completely cut off from the rest of the abdominal cavity, forming a localized, separate compartment. This possibility has been demonstrated by us in some experiments in the study of perforated peptic ulcer. We have shown that this supracolic compartment may be actually squeezed by increasing intra-abdominal pressure in lifting heavy weights. Some of our experiments were as follows: A barium meal was given and the subject was asked to pick up a heavy weight and the barium within the stomach was observed with the fluoroscope. The "magenblasse" or air bubble in the stomach was seen to flatten out as the subject lifted the heavy weight. This we interpreted as due to descent of the diaphragm by taking a deep breath, contraction of the anterior abdominal muscles, and pushing up of the transverse colon and mesocolon, thereby squeezing on the stomach. This shows the more or less isolated subdivision of the peritoneal cavity that the supracolic compartment makes. It is, however, by no means completely isolated from the general peritoneal cavity. In addition, it has connections with the thorax through the subphrenic lymph plexus which communicates by means of lymph vessels piercing the diaphragm with the subpleural plexus on its superior surface. Therefore, pus confined under tension, either in the right or left subphrenic space, is liable to give rise to empyema of infection within the pleural cavity.

A space should be drained of pus or exudate through its most dependent portion. The most dependent portion of the supracolic space is the hepatorenal pouch of Morison. The entrance to this pouch lies lateral to the gall bladder between the lower margin of the liver, which is its superior boundary, and the right flexure of the colon (hepatic flexure). The bottom of the pouch is formed by the reflection of the peritoneum from the superior part of the kidney into the fascia transversalis covering the origin of the aponeuroses of the transversus abdominus muscle below the tip of the twelfth rib. Drainage through a loin incision is the method of choice. However, the drainage tubes

may be brought out through an abdominal incision anteriorly. The lesser peritoneal cavity may be drained through the anterior wall by an incision, either through the gastrohepatic or the gastrocolic ligaments.

The right infracolic subdivision lies above and to the right of the mesentery of the small intestine. It is bounded above by the hepatic flexure and the middle two-thirds of the transverse colon and the corresponding parts of the transverse mesocolon. Laterally, it is limited by the cecum and the ascending colon. At its right inferior angle is the ileocecal junction and the appendix, and at its right upper angle is the inferior part of the duodenum, crossed by the superior mesenteric artery and vein. Leakage from a perforated peptic ulcer and exudates from inflamed organs within the space will gravitate to the right lower quadrant. From here, they may extend upward along the colon into the subphrenic region or downward into the pelvis minor. We have seen that perforated peptic ulcer frequently manifests itself by pain in the right inferior quadrant due to the gravitation of extruded intragastric fluid into this area.

The organs related to this subdivision are the parts of the large intestine which supply its boundary, some coils of small intestines, the inferior part of the right kidney and right ureter, and the inferior half of the descending and horizontal part of the inferior portions of the duodenum. To drain this region at this most dependent point, Penrose drains may be introduced into the right lower quadrant through a McBurney incision. If the pus should be retroperitoneal, an incision in the right loin is preferable, lateral to the ascending colon.

The left infracolic subdivision lies below and to the left of the mesentery of the small bowel, narrows as it passes upward, and reaches to a higher level than the infracolic region on the right side. Inferiorly, it is continuous at the superior aperature of the pelvis with the peritoneal cavity of the pelvis minor. Above, it is bounded by the left third of the transverse colon and transverse mesocolon and still most posteriorly by the pancreas, and laterally by the descending and ileac portions of the colon. At its right upper angle is the duodenojejunal flexure, lying immediately to the left of the vertebral column and in the angle between the vertebral column and the inferior surface of the pancreas. At its left upper angle is the left flexure (splenic flexure) of the colon, while at its left inferior angle is the junction of the ileac with the pelvic colon or the sigmoid colon. This portion of the abdominal cavity contains the majority of the coils of small intestine. In addition, it is related to the inferior third of the left kidney and the left ureter, the lower part of the abdominal aorta, vena cava, and inferior mesenteric and common ileac vessels. Drainage of this subdivision may be established through the left loin or through a tube introduced into the bottom of the pelvis; namely, the rectovesical pouch in the male and the rectovaginal (pouch of Douglas) in the female.

The pelvic space lies upon the pelvic diaphragm below and is bounded by the cecum on the right, the sigmoid colon on the left, and the lower border of the greater omentum above. The peritoneum goes deep into this space. In the female, it covers partially the bladder and uterus and aids the transversalis in the formation of ligaments. Between the uterus and bladder is the uterovesical space; behind the uterus, the pouch of Douglas; and in front of the bladder, the uncovered space of Retzius. These are important surgical landmarks. Pus and exudates gravitate into the pouch of Douglas (posterior cul de sac, Chapter 23) and are sometimes drained through the vagina. This is especially true in pelvic disease. The uterovesical space is important in uterine operations, and the space of Retzius allows the genitourinary surgeons to open the bladder outside the peritoneal cavity. The only communication between the peritoneal cavity and the outside is through the Fallopian tubes.

Thus we see that the general peritoneal space which is enclosed by the horseshoe shaped large intestine and protected in front by the greater omentum is divided diagonally insofar as surgical considerations are concerned by the mesentery of the small bowel.

Therefore, the peritoneum, though not open to the outside (except for the opening to the exterior through the Fallopian tubes), is seen to wind in and out about the intestines (visceral peritoneum) and continue on the anterior and posterior abdominal wall (parietal peritoneum), enclosing a potential space between the two layers. Its extent is said to be equal to that of the skin.

Hertzler estimates the average peritoneal surface in persons averaging 5 feet, 8 inches, in height and weighing 160 pounds as 3,268 square inches (21,986 square centimeters). The cutaneous surface in this group averaged 3,436 square inches (22,167 square centimeters). Its tensile strength and elasticity vary. However, if free from subperitoneal tissue, it will bear a weight of from 1 to 15 pounds.

The peritoneum covers the organs and lines the walls of the abdominal cavity with a few exceptions: the back of the stomach, the caudate lobe of the liver, the left suprarenal gland, the upper surface of the pancreas, and parts of the spleen, left kidney, and transverse colon—all of these, as well as the parietes behind the caudate lobe, are clothed by the bursa omentalis. Therefore, practically all abdominal organs are extraperitoneal. The surgeon will bear this in mind in abdominal operations and he will regard such procedures as transabdominal and transperitoneal, restoring both coverings (visceral and parietal) at the conclusion of the surgery.

Practically the only intra-abdominal organ is the free end of the Fallopian tube and the ovary. The latter is covered by germinal epithelium which is low cuboidal in the adult, and one can see the transition between the peritoneum or the mesothelium and this covering. To all intents and purposes, then, the surgeon should regard his intra-abdominal efforts as subperitoneal in the sense that when he completes his work insofar as possible, he should restore the peritoneal covering which was present before he repaired the organ or removed it. This process is known technically as peritonealization.

Functions of the Peritoneum

The functions of the peritoneum may be summarized under four heads.

Absorptive Powers.—These are due to the capillaries, lymphatics, and macrophages, or tissue-wandering cells. The capillaries of the portal system are more permeable to protein molecules than other capillaries. They may lose these colloids very easily (in ascites) and probably do so normally to a certain extent. The lymphatics are therefore kept busy absorbing this material and returning it to the blood stream by way of the right lymphatic and thoracic ducts. Absorption of colloids (by the lymphatics) and crystalloids (by the capillaries) is rapid and complete. Whole blood and particulate matter are taken up not only by the lymphatics but by the macrophages cells as well. The greater omentum is particularly adept at this, and because of its mobility, it moves or is pulled over to various points of combat, where its capillaries, lymphatics, and cells may absorb great quantities of fluid and semifluid material. Therefore, in spite of the fact that the peritoneum is a closed space, its blood vessels and lymphatics, which extend up through the diaphragm into the mediastinal nodes, provide ample communication with the chest and body as a whole.

Blood clot must be phagocytosed and then the macrophages are carried through the lymphatics to the blood stream. Also a certain amount of decomposition takes place, and the rate of absorption will depend on the extent of reaction produced and the size of the clot. If the clot becomes secondarily infected, as it usually does, the inflammation will, of course, cause an increased absorption, but later this will be slowed down, as is true in inflammation elsewhere. Exudates are absorbed very slowly. This is a defense mechanism and applies to the peritoneal cavity, the pleural cavity, and the tissues in general; that is, the exudate will be absorbed slowly because of the occlusion of the capillaries and lymphatics by thrombi.

Various measures have been suggested to influence absorption. For example, the old Fowler position which consisted of elevating the head of the bed was

thought to delimit absorption. This was based on the idea that absorption was slower in the lower abdomen than in the upper. Recent experiments and clinical observations seem to prove that absorption takes place equally in all parts of the abdomen. It is true, however, that external pressure may play a role. When the abdomen is distended by dilated loops of bowel, as in an acute peritonitis, for example, absorption may be slower, whereas in the less distended abdomen, with much exudate, absorption may be increased.

A frequent observation is that in the intestinal distended abdomens with acute peritonitis, very rapid deflation of the bowel sometimes is accompanied by an increased amount of absorption and an increase in fever and leucocytosis. In a perforated ulcer with gas up under the diaphragm, the exudate may be carried by the free air into this area, and in this way absorption may be earlier simply because the pelvis is farther removed and the flow is upward. The same may be said for pelvic inflammation. It is probably true that the lower abdomen takes care of infection better. However, it is believed by many observers that this is due to the fact that the distance traversed by the infecting agent will be greater in the lower than in the upper abdomen.

The idea of introducing large quantities of saline into the peritoneal cavity and thereby converting the peritoneum into a secreting area rather than an absorptive area in the treatment of peritonitis has been largely disproved. Although it is true that if large quantities of fluid are given intravenously the hydrostatic pressure will be increased and the osmotic pressure decreased, fluid will find its way into the peritoneal and into the pleural or pericardial cavities as well. The Fowler position also is not to be desired because of the danger of thrombophlebitis and phlebothrombosis which may result from the angulation of the ileofemoral veins. Since there already is a stasis due to immobility, the predisposition toward thrombosis is increased by this position. In peritonitis there is also hemoconcentration due to the loss of large quantities of plasms into the peritoneum (Chapter 14). The Fowler position does not in any way influence absorption from the peritoneum, nor does gravity cause exudates to accumulate in the pelvis. This famed position predisposes to thrombosis and possible embolism and, in addition, it makes the patient extremely uncomfortable so that he cannot turn freely or breathe easily. It is therefore better to let the patient lie in bed and turn from side to side, moving his arms and legs. By introducing large quantities of saline intravenously, the peritoneum may be converted into a more or less leaky mesothelial lake, but it must be borne in mind that all tissues will become edematous, including the bowel wall and bowel distention.

It is a well-known fact that the peritoneum is an excellent dialyzing membrane which is permeable to solutes and crystalloids. The transudation of solutes into the peritoneal fluid is probably one of the mechanisms used by the body in an attempt to excrete certain toxic substances. This physiological function of the peritoneum may be used in the treatment of disease. Peritoneal irrigation makes possible the use of its dialyzing capacity for the removal of diffusible substances from the plasma and ultimately from the extracellular fluid. The irrigating fluid will not cause a depletion of plasma constituents below normal levels if a proper adjustment of the concentration is maintained. In an effort to accomplish this extrarenal pathway or excretory function, a modified Tyrodes solution was used. This contains sodium chloride, 8 Gm., potassium chloride, .1 Gm., magnesium chloride, .1 Gm., sodium acid phosphate, .05 Gm., sodium bicarbonate, 1 Gm., and dextrose, 1½ Gm. It was prepared in large volumes by Fine and co workers. Incisions were made in the upper and lower abdomen for the purpose of irrigating the peritoneal cavity. The chief danger of this method is the injury to the peritoneum; also the fact that any foreign body within the peritoneal cavity is soon walled in by adhesions. To overcome this, heparin has been used to prevent formation of fibrin, and penicillin is used in prophylaxis against infection. Sodium sulfadiazine should not be used because of the danger of further renal injury. In this way large quantities of fluid may be used to irrigate the peritoneal cavity. We have had one case of total anuria in a woman who was Rh negative and gave birth to

an Rh-positive fetus with erythroblastosis. This woman was in profound coma and had a complete anuria. The peritoneal irrigation, we thought, had something to do with her ultimate recovery. However, in her case the use of plasma intravenously seemed to help draw fluid from the tissues which were edematous and permitted large quantities of the fluid to find their way through the peritoneum to the outside. Ultimately the kidneys began to function again.

In inflammations of the peritoneum not only are crystalloids and colloids lost, but, in addition, large numbers of leucocytes. We have frequently called attention to the fact that in the face of an extensive peritonitis, the blood leucocyte count may be low. This is undoubtedly due to the large volume of leucocytes that are lost from the circulating blood into the peritoneal cavity. It is surprising that after removing the focus and draining or merely draining, localization is facilitated and the blood count goes up. It has been observed further that after the cause of the peritonitis has been removed, such as a perforated appendicitis, the blood count will rise as the peritonitis subsides. This is almost conclusive evidence that the cause of the leucopenia was the large number of circulating white cells which were lost in the peritoneal cavity. One last statement should be made concerning the so-called secretory or excretory function of the peritoneum. The older surgeons thought that by putting multiple drains in the abdomen and giving large quantities of fluid intravenously, they could convert the peritoneum from an absorbing membrane to a secretory membrane. They also thought that by using the Fowler position and putting most of the drains in the lower abdomen that they could actually reverse the flow. All of this has been fairly well disproved. We have just noted how difficult it is to use the peritoneal cavity as an irrigating membrane when large volumes of solution are forced through. It is even more difficult for nature to accomplish this when multiple drains are inserted. In fact, these drains are soon walled in by a fibrinous exudate so that they drain only a small area immediately surrounding them. With this in mind, the modern trend has been to reverse the old doctrine, "When in doubt, drain" to "when in doubt, do not drain."

Drainage is employed for definite walled-in abscesses or collections or exudate rather than for prophylaxis or with the idea of draining the peritoneal cavity. This concept rests upon the fact that in addition to the almost useless function of a drain, it is a foreign body which will encourage dense adhesions. There are some exceptions to this statement: As a preventive measure in cases where the base of the appendix and cecum are necrotic, a cecostomy and, in addition, soft Penrose drains are used; in perforated appendicitis, the pelvis and right colic gutter are drained to permit exit of exudates; following gall bladder surgery where there is danger of leakage and bile peritonitis, drains are used, although even here some surgeons are now abandoning this type of drainage. Preventive drainage is used only for short periods (twenty four, forty-eight hours). Drainage of a definite abscess follows the rules of absces elsewhere.

Reparative Powers.—We have seen in Chapter 3 how quickly and completely the peritoneum heals. Within one-half hour the suture line is impermeable to fluid and gas, unless these are under pressure. Although the peritoneum is one cell layer thick, it quickly repairs defects due to trauma or disease. Repair here is exactly like repair elsewhere. Fibrous tissue is covered by mesothelium and, if healing is by first intention, a minimal scar is formed. In the presence of severe trauma or infection, repair is by second intention; that is, there is much more scar tissue and often there are dangerous or vicious adhesions or bands. Its modus operandi is by adhesions. These may form between loops of bowel or between the bowel and the parietal peritoneum, or between the bowel and solid organs. These adhesions "splint" the part, or put it at rest, prevent leakage, and allow for complete healing. Then having finished their task, they stretch into bands or sheets, lose their blood supply ultimately, because of this stretching, and are absorbed. This is the reason surgeons will not cut adhesions that are less than three years old, unles they are

dense or in such positions that obstruction results. New adhesions have straight, parallel vessels; congenital bands have networks of capillaries. The greater omentum always takes part in this repair, "splinting" the part, reinforcing the freshly made collangenous tissue, localizing the site of surgery, or injury, or disease, until it is well. Indeed, the greater omentum is the "policeman of the abdomen" and the "surgeon's friend." For this reason the surgeon uses it to cover over the field of operation. It may be seen then, that, contrary to popular opinion, adhesions are indispensable to repair. However, should there be much trauma to tissue, or extensive infection in the peritoneal cavity, these adhesions, like deep injuries to the skin, will be dense and vicious, leading to interference with intestinal function and often obstruction.

The normal covering of the abdominal organs is peritoneum. When a raw surface has been made, it should be covered, just as in the skin, to avoid dense scars. Lacking peritoneum, we may use the omentum as a pedicle or free graft. If this is not available, tabs of mesenteric fat, appendices epiploicae, the broad ligaments, or other available mesothelial-covered structures are used.

Powers of Resistance (Immunity).—The peritoneum, like the pleura, is a mesothelial membrane one cell layer thick, yet its powers of resistance are great (see Chapter 19). This is possible because of local immunity in terms of cells, and although we have no proof for the statement, we are coming to believe that all of these cells may under stress become or give rise to macrophage cells. In experimental animals, pure cultures of bacteria, when introduced into the peritoneal cavity, fail to cause peritonitis. Should the bacteria be implanted in bits of agar or pieces of liver tissue, or should the peritoneum be ruthlessly traumatized, peritonitis results. This explains the surgeon's ability to perform bowel operations without infection in the absence of gross contamination.

It was formerly thought that different portions of the peritoneal cavity manifest a difference in their defense reactions. This gave rise to postures in the treatment of the disease, varying from the Trendelenburg position to favor the reabsorption of the products of the peritoneal effusion and hemorrhage to Fowler's position to hold back the absorpiton of such products. Today we no longer believe in these theories. In fact, the peritoneum manifests the same degree of resistance in all parts of the abdomen. Formerly it was thought that the pelvis had a very high degree of resistance as compared with the upper abdomen. This is due to the fact that the pelvis is frequently the seat of gonococcal infections which have a tendency to become localized. It was noted at the same time that should the pelvic viscera be infected with the streptococcus, the same degree of virulence occurred as was present in any portion of the abdomen. Also, it was formerly thought that infections in the upper portion of the abdomen were particularly virulent because the diaphragmatic peritoneum allowed for almost a spongelike absorption. It is probably more in accordance with the facts that deaths following biliary operations are due to traumatic injury of the liver rather than to any special condition of defense or increase in absorption from the diaphragmatic peritoneum. Also, failures of esophageal surgery and stomach surgery were thought to be due to the lowered resistance of the upper abdomen. There is no basis of proof for this. It is more nearly correct to assume that failures occurred because of leakage or occlusion of the neostomies or because intestinal loop herniations with intestinal obstruction, or just as they do in modern surgery if careful techniques are not employed.

The concept of many of the observers today is that the peritoneum possesses an extraordinary capacity for defense throughout all sections of the abdominal cavity and, here, as elsewhere in the body, it is the particular immunity of the individual locally and generally and the virulence of the invading organism, together with the particular intensity and speed of aggression, which determine the gravity of the process within the abdominal cavity rather than any special capacity for the various portions of the peritoneum to withstand the infection.

The Fowler position formerly was thought to have at least one redeeming feature; namely, that of keeping the patient in a semisitting position, as at least exudates would gravitate down into the pouch of Douglas or the pelvis minor. Even this seems to be more or less hypothetical because it *is a well-known fact that the routes that* exudate will follow are the anatomical planes which have been explained previously in this chapter.

Recent experimental work has shown that the peritoneum does not respond in portions. It is customary to speak of localized peritonitis, a spreading peritonitis, a diffuse peritonitis, and a general peritonitis. These are terms which describe gross reactions rather than pathological entities. The entire peritoneum probably responds as a whole. It is true that the focus may show the greatest degree of reaction. However, the entire peritoneal cavity immediately begins to pour forth large quantities of peritoneal transudate and exudate to help the particular area which is involved. Later, it is perhaps correct to use the term localized peritonitis which abscess is formed. In this way the peritoneal cavity behaves very much like a cellulitis caused by the streptococcus or the staphylococcus prior to localization. The peritoneal cavity is able to cope with ordinary infections unless it is severely traumatized. Its methods of defense depend on local factors in addition to those found elsewhere in the body, as mentioned in Chapters 4 and 5.

Sensory and Motor Nerve Power.—Generally speaking, the parietal peritoneum is supplied with sensory nerves through the intercostal nerves. (See Chapter 18.) Thus, the pelvis is supplied by the twelfth intercostal and first lumbar nerves, and sensory impulses enter the cord at the twelfth thoracic and first lumbar spinal segments. Therefore, pain from the parietal peritoneum is accurately located (although it is referred to the spinal segment involved and hence may be confusing). The visceral peritoneum is only sparsely supplied with sensory nerves, and these apparently run with the sympathetic (splanchnic) nerves. Therefore, pain in the intestines is more general and less accurately located, occurring when tension or crushing force is applied over wide areas. Trimming a colostomy or crushing a spur does not cause pain. Furthermore, the mesentery probably contains most of the nerve supply. This explains why the surgeon must not pull on the mesentery while doing abdominal operations under local anesthesia. However, the greater omentum seems devoid of nerves, yet if pulled on or separated from inflamed viscera, pain results. Violent peristaltic waves produce general, cramplike pains. The early pain in appendicitis may be referred to the epigastrium, through the twelfth spinal segment. Should the parietal peritoneum become involved, pain would be present in the diseased zone. The physician must bear these facts in mind when making a diagnosis of intra-abdominal disease. In addition, there are motor nerves to the peritoneum—not to the membrane itself, but to the protecting muscles over it. Thus, in appendicitis there are pain, tenderness (which is always a more accurate diagnostic sign), and involuntary muscle spasm or rigidity. *By these symptoms* and signs the physician may usually diagnose the site of the lesion, and if the organ is normally situated, locating the site means diagnosing the organ involved.

From the foregoing discussion it would seem that the supply of sensory fibers to the viscera is very small in comparison with other parts of the body. Only about one-fourth of the fibers of the splanchnic nerves are sensory. The pelvic (nervi erigentes) and vagus nerves whose function is more closely related to somatic parts and cerebrospinal innervation, are composed of about one-third sensory fibers. The cell bodies of the sensory visceral nerves are located in the dorsal root ganglia and ganglia of the *cranial nerves.*

Visceral pain is experienced when the nerve endings in the musculature of submucosa of the hollow viscera are stimulated by stretch or pressure. Sudden distention and marked contraction constitute adequate stimuli. These stimuli produce some degree of anoxemia which sensitizes the visceral pain nerve endings. The same is true of inflammation. Pain from the viscera is not well localized and is usually referred to the

surface of the body, innervated by the cerebrospinal nerves originating in those segments of the cord which innervate the viscera. Therefore, in interpreting referred pain, it is important that we know the course of the nerve supply of the viscus and its embryological history as well. An example of this is cited by Ivy who states that pain experienced on irrigation of the right central diaphragmatic pleura is referred to the right somatic area innervated by the third and fourth cervical segments which would be the upper shoulder. However, irritation of the right lateral diaphragmatic pleura may cause pain to be referred to the tenth and eleventh thoracic segments or the appendiceal region. This wide difference is related to the embryological development of the diaphragm which receives a contribution from the third cervical to the twelfth thoracic segment. According to Ivy, the types of pain observed in viseral disease may be grouped under five heads:

1. True visceral pain due to irritation or stimulation of true sensory pain nerve endings in the viscera which is accurately localized by the patient. With training, one can learn to localize with an accuracy of one or two inches the points stimulated in the esophagus, stomach, or duodenum and the jejunum. This phenomenon is related to the experienced learning or conditioning which enables one to localize or project a prick of the finger or the back of the hand to those areas even when the subject is blindfolded. Because of the small number of sensory nerves to the viscera, some individuals will be slightly devoid of visceral sensitivity. These are the persons who will have a silent peptic ulcer and a silent cholecystitis and so forth. Ivy believes that true visceral pain pathways are present in the spinal cord that send impulses to the cerebral cortex for perception. Other observers do not believe that such paths exist. According to the other theory, visceral pain is due to a spread of visceral impulses to the primary or secondary somatic pain neurons in the dorsal root ganglion on the dorsal gray horn, or to viscerosomatic (visceroskeletal) reflexes which cause muscle rigidity or spasm or reflex vasomotor or metabolic changes which in turn stimulate somatic pain nerve endings in somatic tissues. Stated in a different way, these two theories imply that (a) the visceral impulses will find their way through somatic pain neurons in the dorsal root ganglion or the dorsal gray horn or (b) by causing a reflex motor activity in muscle, causing spasm or causing reflex vasoconstriction, pain is referred to the site where such reflex activity occurs. The Lange-Ross theory holds that the impulses go to the dorsal root ganglia cells, and on reaching the gray matter of the dorsal horn, the impulses pass to the secondary neuron of the somatic pain nerves of these segments. This results in the cerebrum interpreting the pain as coming from the segment innervated by the primary somatic pain nerves. MacKenzie holds that true visceral pain does not exist and that the disease process in the viscera gives rise to the increased stimulation of the nerves passing from the viscera to the spinal cord. This increased stimulation affects neighboring centers and so stimulates sensory, motor, and other nerves that issue from this part of the cord. He refers to the stimulation as a viscerosensory reflex, although this is not really a reflex. The expression visceromotor reflex which is used to explain muscle rigidity is a good physiological expression. It is very probable that a true visceral pain pathway exists which makes connection with the cerebral cortex. It is also possible for visceral pain impulses reflexly to cause changes in the somatic tissue which in turn stimulate somatic pain nerve endings.

2. Referred pain in which the pain is not localized in the diseased viscera but in the somatic part deeper than the superficial surface of the skin, the somatic part to which the pain is referred being related phylogenetically to the innervation of the viscera. Head taught that sensations arising from an area of low sensibility are interpreted by the cerebrum as coming from an area of higher sensibility. As an example, if a patient with tabes is pricked in a cutaneous area of low sensibility, he reports that it comes from an adjacent area of higher sensibility which may be located at some distance from the site which is stimulated. According to the theory of the existence of true visceral pain, stimulation of the central portion of the diaphragm

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that holds the intestine in position by its attachment to the posterior wall of the abdomen. For the small intestine, its root runs roughly from the upper left hypochondrium to the lower right pelvic area and then spreads like a fan to serve approximately twenty-five feet of intestine. It carries the blood supply, nerve supply, and lymph ducts (lacteals). Should it be severely injured, or divided, the corresponding loop of bowel would die, for the vessels are terminal ones, with few anastomoses. The mesentery of the large bowel is known as the mesocolon, the mesosigmoid, etc. *Ligaments* are strong *folds of peritoneum holding solid organs in* position. Examples are the broad ligaments of the uterus, the lienorenal ligament, etc.

Inflammations of the Peritoneum

Should the peritoneum become inflamed, a grave condition ensues. The general term peritonitis is used to denote any inflammation of the peritoneum whether it be local, from which recovery is the rule, spreading, which carries a higher mortality, or general, which is invariably fatal. Furthermore, it is necessary to know whether its origin is bacterial or chemical, and if the former, what the causative agent is, because *different types require different treatment and presage different prognoses.* Individual bacterial types are often impossible to diagnose until an operation is performed and the cause and type are clearly seen or discovered by smear or culture. Even the chemical variety has various causes which are treated differently and also give rise to diagnostic problems. Of the bacterial types, pyogenic bacteria (*Bacillus coli communis,* staphylococci, and streptococci in combinatoin) are the most common offenders, giving rise to pyogenic peritonitis. However, other organisms, particularly the anaerobes, are frequently found. Rarely, actinomycosis is the cause. This usually originates from an intra-abdominal suppurative lesion such as perforative appendicitis or perforative diverticulitis but may occur after traumatic rupture of the bowel, gangrene with perforation, following mechanical obstruction, and even postoperatively (after intestinal surgery) from infection introduced from the outside or excessive handling of devitalized bowel.

The inflamed peritoneum is soon covered with a fibrinopurulent exudate, which in turn is bathed in pus. The loops of bowel are distended, for the exudate limits preistalsis. The greater omentum attempts to act as a pyogenic membrane, and with the matted loops of bowel it usually succeeds in producing a localized peritonitis, with or without abscess. This is frequently seen in perforative appendicitis. Should the infection spread beyond the immediate environs of the appendix (spreading peritonitis), the omentum with new loops of matted intestine may limit it or may fail to do so, with resultant general peritonitis. Then the visceral and parietal peritoneum is red, covered with a fibrinous exudate, loops of distended bowel lie motionless and adherent to each other, the omentum lies unattached, and pools of pus are found in the various dependent portions of the abdomen and between intestinal loops.

General Effects of Secondary Peritonitis.—The surface area of the peritoneum is about equal that of the skin surface. Therefore, a truly

which embryologically originates from the third, fourth, and fifth cervical segments causes impulses of pain which pass up to the portion of the cerebrum which receives pain impulses from the somatic tissues innervated by the third, fourth, and fifth cervical somatic sensory nerves. So the cerebrum interprets on the basis of Head's law, the pain as originating in the shoulder area. The same is true in the lateral diaphragmatic pleura; the impulses pass into the tenth and eleventh thoracic segments. Since the nerves from these segments innervate the somatic areas around the appendiceal region, the cerebrum interprets the pain as coming from the right lower quadrant of the abdomen.

3. Habit reference of pain in which the pain from a newly located focus is referred to an area sensitized by previous disease or injury. For example, the patient has had gall bladder disease or injury and then develops appendicitis. The pain in the early course of the appendicitis is referred to the gall bladder area. This phenomenon is particularly important in cardiac diseases as simulated abdominal disease or the reverse. If a patient has had previous attacks of epigastric pain due to ulcer and then suddenly develops a severe pain, one thinks of not only ulcer but cardiac disease referred to the ulcer area because the patient has had previous experience with ulcer pain. Indeed, some cardiologists state that most acute coronary disease is thought by the person to be merely acute indigestion because he has had experience with the latter.

4. Secondary visceral or referred pain in which the disease of one viscus causes reflex functional disturbance in another which in turn gives rise to pain in an area not primarily diseased. For example, disease of the appendix causes pylorospasm and the pylorospasm causes pain in the epigastrium. Another example of this is the type of pain experienced in kidney colic which at first causes a reflex ileus. Pain is referred to the distention of the intestines rather than to the particular site of the obstruction to the urinary tract. Later the pain is actually localized at the site of the obstruction.

5. Associated somatic pain. This, according to Harvey, is pain in which the disease of the viscus spreads to involve adjacent somatic nerves or to involve the parietal serous surfaces; that is, the parietal pleura or peritoneum which are innervated by somatic pain nerves. This is seen in cases of appendicitis in which the viscus is inflamed; later the overlying peritoneum becomes inflamed, causing neighboring nerves to become involved. Pain is projected along the course of those nerves.

In summary, it might be well to point out that visceral pain is not accurately located by the patient, yet it is one of the most important guides to disease processes. Therefore, the physician in making a diagnosis must remember that the pain may be referred—that it may be a habit reference or a secondary visceral pain or an associated somatic pain. With these in mind he will more nearly arrive at the correct interpretation of the pain. Many examples of this could be cited. However, in the various portions of this chapter the phenomenon of both types of pain will be recorded in connection with the subjects discussed.

The greater omentum is a double layer of peritoneum hanging in apron fashion from the greater curvature of the stomach. As indicated, its importance cannot be overemphasized. In infants it is extremely thin, devoid of fat, and filled with tiny blood vessels. In the adult it becomes filled with fat and is much thicker. Its functions are the functions of the peritoneum greatly amplified, and its movability makes these functions available to all parts of the abdomen. Hertzler studied the migration of the omentum through windows and by x-ray after fastening small shot into it. He believes that the fibrinous exudate at the site of inflammation and the hyperemia of the peritoneum about this area are accompanied by a similar response in the omentum. Thus the omentum becomes a movable tissue filled with leucocytes which are drawn to the field of battle as are other leucocytes, perhaps by chemotaxis. In extremely virulent infections there are few leucocytes in the omentum and no migration occurs. The mesentery is the double layer of peritoneum

polymorphonuclears. This is also very variable, particularly in children. However, even in adults a large proportion of the circulating leucocytes may be within the peritoneal cavity, giving a very low white count. In general, the patient will be ill at ease and worried about his condition. His flexed knees, short breath, distended abdomen, anxious and pinched expression have given rise to the famous "hippocratic facies." The symptoms and signs are due to the underlying pathological conditions (namely, that of a widespread infection together with that of an intestinal obstruction) and therefore they vary with the preponderance of the various components and their effects.

The treatment is based upon ample experimental and clinical experience. Obviously most important is prevention, if possible. This can be done by prompt attention to the cause: appendicitis, gall bladder, perforated ulcer, etc. In case of local, spreading, or even general peritonitis, if the patient's general condition permits, the focus is removed if possible and adequate drainage instituted (although the Penrose or other drains are soon walled in as are other foreign bodies). Much has been written recently on the delayed treatment of spreading peritonitis secondary to perforative appendicitis. Those who favor it invoke the dictum previously quoted in this book: "Wait for localization." Those who oppose it are guided by the rule also given in these pages: "If an acute focus can be removed, spreading of the infection may be avoided and septicemia averted." No hard and fast rule can be given here. Each patient must be individualized. However, there is a happy medium between the extremes, since no operation has merit enough to be used on a patient who cannot stand it. Therefore, the desirable method of procedure is adequate preparation and gentle nontraumatic surgery following this preparation (whether the preparation takes one hour or a week). Lengthy traumatizing procedures must be avoided; they simply add to the shock, as would an extensive scrubbing in a severe burn. In all cases, adequate attention should be given to the fluid balance and blood transfusion used if necessary. This is done before any surgical intervention is attempted. Morphine is given at four-hour intervals until the respirations reach 12 per minute, and no food is taken by mouth, so that the intestines are at rest completely. In addition, the use of the Levine duodenal tube aids greatly in dealing with the ileus. This tube is attached to a suction apparatus (Wangensteen) so that the distended intestines may be decompressed. With this in place, frequent sips of water are given to moisten the throat and test the patency of the tube. Sometimes irrigation of the tube with warm salt solution is necessary. Heat to the abdomen may be helpful as a part of the complex treatment of this disease.

Occasionally, the surgeon will elect to decompress the bowel by direct opening (enterostomy; Witzel's operation; or appendicostomy) under local anesthesia. This is useful where there is, in addition to the

general peritonitis would be comparable to a 100 per cent burn and would be invariably fatal. Fortunately, the extensiveness of peritonitis is not apt to reach this proportion. However, since the peritoneum responds as a unit to infection, should the inflammation involve large areas or persist, the general effects would be similar to an extensive burn.

The large area of inflammation may result in (1) the loss of copious amounts of blood plasma, water, and electrolytes, (2) hemoconcentration, hypoproteinemia, hypochloremia, and reduction of circulating blood volume, (3) stagnant anoxemia as a result of (2), (4) paralytic ileus due to the exudate on the peritoneum and swelling of the bowel wall as in inflammation elsewhere, (5) anoxic anoxemia from the distention because the diaphragm cannot descend and the lungs cannot function properly, (6) anuria due to the preceding changes, (7) pulmonary edema, (8) toxemia, bacteremia, and hemoconcentration which cause the destruction of large numbers of erythrocytes, resulting in persistent anemia which is not detected by hematocrit readings because the circulating blood volume is greatly reduced with a relatively increased amount of plasma lost, giving the picture of hemoconcentration. Secondary effects include azotemia and edema as a result of anuria and alkalosis if vomiting persists.

The general effects vary with the suddenness of the inflammation and the area involved. Thus, a large perforation of the stomach or duodenum from ulcer or the cecum at the base of the appendix from appendicitis or any part of the alimentary canal due to penetrating or perforating wounds may flood the peritoneal cavity, inducing an extensive rapid inflammation, causing profound shock. The insult may be due to chemical mechanical, or bacterial causes with the same effect. If the inflammatory changes are evolved slowly, as in tuberculous peritonitis, general effects are barely perceptible. In between these extremes are the more common varieties of peritonitis which cause milder, but none the less apparent, changes. The symptoms and signs depend upon the extent and therefore vary from pain, tenderness, and rigidity, with slight or no systemic symptoms, to generalized abdominal pain and euphoria just before death. The patient vomits stercoraceous material continually, there is no passage of flatus or feces, and the abdomen is distended and absolutely silent on auscultation. Soon there is marked dehydration, as a result of paralytic ileus.

Symptoms and Signs of Peritonitis.—The fever is high, ranging up to 103° F. and above in adults and up to 105° F. in children. There are great variations in the degree of fever, sometimes ranging up to 106° F., and where there is an overwhelming infection, the temperature may be subnormal. This is particularly true in cases of large perforations of the bowel due to gangrene or due to a large perforated ulcer or in septic abortions. In such cases the temperature may be subnormal and all the symptoms and signs of shock may be present. The leucocyte count is usually high, being about 20 to 25 thousand, with 80 to 90 per cent

albumin-globulin ratio. The serum globulin may be high and the serum albumin low, and yet the total serum protein may be normal or even above normal. However, if the volume of total protein is low, the indications are clear. In addition, blood chlorides may be run whenever indicated. It is our custom to alternate between distilled water with glucose and physiological saline with glucose so that we may avoid hypernatremia. Also the use of multiple vitamins within the fluid at least once a day has, in our opinion, helped to care for the vitamin requirements. It is not our custom to place a cannula in a vein and leave it there except in newborn babies and very small infants, and even here we have found that it is advantageous to use a very fine needle and introduce this needle within the ankle or scalp vein. In all adults, it is our custom to rotate, using a different vein of small caliber to avoid thrombosis of a larger vein. We do not use hypertonic solutions as explained in Chapter 11, and arm veins are preferred so that phlebothrombosis may be avoided in the legs.

Peritonitis is a treacherous disease and even though early complications may be successfully met by the treatment outlined, later complications frequently require secondary operations. Among these may be mentioned late types of obstructions where exploration may be indicated. Although the early types of obstructions may be successfully handled by the Miller-Abbott tube with suction or Witzel enterostomy, a late obstruction may be due to an organized band which may require open operation with exploration of the abdomen.

Pelvic abscess is suspected when the fever becomes intermittent or remittent with chills, and then after the peritonitis has subsided, a persistent diarrhea. This is due to irritation of the sigmoid or rectum by the abscess. Careful rectal or vaginal examination should be done routinely when the progress is not satisfactory. Such an abscess may have to be drained from above or through the cul-de-sac or rectum.

Subphrenic abscess manifests itself also by the symptoms and signs of pus under pressure. In addition, there will be a descent of the liver with an elevation of the diaphragm and an increase in the liver dullness. Fluoroscopic examinations aid greatly in the diagnosis by indicating elevation and fixation of the diaphragm. The treatment is that of abscess elsewhere; namely, wait until localization has occurred and then institute adequate drainage. This is done by resecting a small section of the tenth rib. The pleura is pushed up and the diaphragm is stitched to the chest wall, if not adherent, and drainage is instituted. When the abscess is very large, this may be accomplished through the subcostal region. If the pleura is not adherent, the two layers of the pleura may be sutured together at the costophrenic angle, and after the two layers of pleura have become adherent, drainage may be instituted, thereby avoiding contamination of the pleural cavity.

Idiopathic peritonitis, or primary peritonitis, is caused as a rule by the streptococcus or pneumococcus.

peritonitis, a closed loop of bowel or an obstruction low in the ileum or colon, although these can usually be decompressed by the Miller-Abbott tube.

Congestion at the base of the lungs, with pulmonary edema or complicating patchy pneumonia, is not uncommon in peritonitis. This is due to the bowel distention and sometimes an involvement of the undersurface of the diaphragm. Either cause limits the movements of the diaphragm and increases venous stasis within it, further limiting its motion. In addition, there is stasis in the pulmonary veins. Due to the low plasma content of the blood, the increase in venous pressure, and increase in the negative pressure within the thorax due to dyspnea, fluid exudes into the alveoli. Exudation is increased when large amounts of intravenous fluid are introduced. Respiratory difficulty results and there is cyanosis. This state may be relieved by frequent blood transfusions to increase the osmotic pressure, frequent turning in bed, deep breaths, and the use of oxygen inhalations. The latter are said to aid in the absorption of gas from the bowel.

Attention to the primary cause of the peritonitis takes precedence over all other forms of treatment, and the restoration of water balance and the electrolytes and the replacement of blood volume make this possible. In addition, the use of chemotherapeutic agents and antibiotics to combat the infection offers very much to the management of the disease. The use of penicillin in large doses, namely, 100,000 units intramuscularly every three hours, together with 300,000 units with each intravenous injection, will give the patient approximately a million and a half units a day if 3 liters of fluid are given. In addition, streptomycin up to 2 or 3 Gm. in twenty-four hours, given intramuscularly is advantageous because peritonitis, as we have said, is due not only to cocci, but also to bacilli of the gram-negative group. Sometimes sodium sulfadiazine is given intravenously since the drug cannot be given by mouth. But its possible effects on the kidneys must be remembered. There is no question about the efficacy of chemotherapeutic agents and antibiotics in the treatment of peritonitis, no matter what the cause.

The criteria for the use of physiological saline and glucose, distilled water with glucose, plasma, and whole blood have been evaluated in previous chapters on hemorrhage, shock, and water balance. It may be recalled that a good clinical rule is as follows: If the patient is eliminating an adequate amount of urine with a normal specific gravity and if, in addition, the skin and mucous membranes are moist and the temperature is falling, then the patient is probably receiving adequate amounts of fluid. To substantiate this further, a daily hematocrit and plasma protein may be run by the copper sulfate method. This is an inexpensive and quick method of great accuracy, so that the degree of hemoconcentration and level of plasma protein may be estimated. There is one omission in determining the plasma protein by this method; that is, the

there may also be generalized pain. (2) In an age of less than 3 years, initiation of the illness by a chill is suggestive of the primary peritonitis and yet we have seen pyleophlebitis accompanying appendicitis in children of this age. (3) Leucocytosis is usually higher in the primary form. However, here again, appendicitis simulates it. Pneumonia may closely resemble primary peritonitis, and it may be an accompanying feature. Both may be present at the same time. The x-ray of the chest may be helpful.

Because of the difficulty in diagnosis, exploration is usually indicated; however, not until fluid balance has been restored, transfusion has been given, large doses of penicillin administered. Exploration is usually done under local anesthesia through a small incision. If the surgeon encounters the type of exudate which has been described, he will immediately make a smear, and if a pure culture of streptococcus is encountered, a small Penrose drain will be inserted. There has been a great deal of questioning about the use of this Penrose drain. It has been said that this is superfluous because it is impossible to drain the entire peritoneal cavity, and if it is primary peritonitis, this is unnecessary. Indeed, if one were absolutely sure of the diagnosis, even this small exploration would be superfluous and unnecessary. But even after opening the abdomen, one may be in doubt. It would be wrong to explore too thoroughly such an abdomen, and since trauma accentuates the inflammation, actually the operation would have dire and serious effect. Therefore, it is our practice to introduce two or three small Penrose drains and by so doing, if the diagnosis is an error, drainage about the appendiceal area may prevent further complications. If the diagnosis is correct, drainage of this type does no harm. The care of the patient is the same as in other types of peritonitis with the use of large doses of penicillin given intravenously and intramuscularly. In addition, if the pneumococcus is at fault, sodium sulfadiazine may be helpful.

Mesenteric lymphadenitis is a definite clinical entity. It is usually seen in children. The mesenteric nodes (particularly the lower ileac group) are enlarged and swollen. Sometimes the entire small bowel mesentery is involved. Sections and cultures reveal an inflammation, with polymorphonuclear cells, but no specific organisms have been found. It is probbaly a virus disease related to the upper respiratory infections. The lymphoid tissue in the nose and throat and in the ileum and appendix as well as the lymph nodes is involved. The symptoms are vague. There are diffuse abdominal pain, nausea, and slight elevation of temperature. The leucocyte count is normal or there may be leucopenia. If extensive in older children, a path of tenderness roughly overlying the mesentery of the small bowel may be elicited. The difficulty of distinguishing this disease from appendicitis is obvious, since a swelling of the lymphoid tissue of the appendix is part of the process but not its cause. The condition is benefited by opening the abdomen rather than by the appendectomy which is usually done.

The term primary peritonitis may be questioned since the disease is rarely primary. Another name is metastatic peritonitis, indicating that it reaches the peritoneum from a focus outside the abdominal cavity. The cause of the condition is usually the streptococcus or the pneumococcus, although other organisms may be at fault, such as Friedländer's bacillus.

The etiology is often very obscure. It is thought that the organisms gain entrance in the females through the genital tract by the way of the uterus and tubes. Since the disease occurs in males, this cannot be the only avenue of entrance, and there is no evidence to show that such ascending infection takes place. The gastrointestinal tract may be the source of infection, and the pathological studies have shown severe inflammation of the small bowel, especially the terminal ileum. Pneumococcic peritonitis may result from diaphragmatic invasion by way of the thoracic lymphatics; however, this would imply a descent against the lymphatic current. In most instances the infection gains access to the peritoneum by way of the blood stream. This is true because upper respiratory infections are usually forerunners and bacteria may be found in the blood stream in such cases.

The pathology of the disease is typical of general peritonitis. The general peritoneal cavity is acutely inflamed. When the abdomen is opened, there is a flow of serosanguineous fluid, if the cause is streptococcus, or a flaky exudate if pneumococcus. There is no odor to the pus, and if a swab is taken of the exudate, a pure culture of the streptococcus or pneumococcus is obtained. The visceral and parietal peritonea are involved and no focus is found.

Symptoms and Signs.—The disease occurs about equally in males and females, usually in children. Also usually, but not invariably, it follows upper respiratory infection. Sometimes there is diarrhea. Since the diarrhea in infants and children is so commonly due to gastroenteritis, it offers challenging symptoms to explain. Often the forerunner is referred to as "intestinal flu." The older children will complain of abdominal pain which is diffuse and is not localized, nor does it localize after careful observation. There are high fever and vomiting, which are persistent. The temperature reaches 104 to 105° F., the abdomen is tender, and the pulse is fast. In the older individual there is a great deal of rigidity, but in babies the abdomen may be soft. There is usually some degree of distention, and the abdomen is practically silent, although in children this may vary. The white blood count is extremely high, from 20,000 to 40,000. The red count is increased due to dehydration.

The differential diagnosis lies largely between primary peritonitis and secondary peritonitis due to a perforated appendicitis. It is true that in perforated appendicitis, there are distinguishing features of the disease, such as the following: (1) In appendicitis there is maximal pain on the right side, while in primary peritonitis there is pain and tenderness generally, but this does not offer much help in early appendicitis;

appendix, with a large hole near its base, and outpouring of fecal matter, or acute pancreatitis; occasionally one sees a picture which clinically mimics intestinal obstruction or coronary occlusion.

The cause of the condition is usually leakage following surgery or following acute cholecystitis, subsequently causing gangrene of the gall bladder and perforation. This indeed has been the reason advanced for immediate operation in acute cholecystitis. This will be discussed at the end of Chapter 22. It is not always possible to demonstrate a gross defect in the biliary system in bile peritonitis. We have seen several patients in whom at autopsy no definite perforations could be seen in the biliary tree, yet a generalized biliary peritonitis was present. Both of these had a passive congestion of the liver and the spleen, pulmonary congestion, and cholelithiasis. In most traumatic conditions of the liver, the danger of bile peritonitis is always present.

The treatment of bile peritonitis is, of course, prevention if possible and immediate drainage as soon as the condition is recognized. Recently we have seen two cases with complications who have had gall bladder surgery with closure of the abdomen without drainage. Both had what was thought to be ascites; paracentesis showed the fluid to be bile. Instead of making an incision to drain the abdomen, repeated paracenteses were done, and both recovered. They subsequently developed strictures of the common bile duct which required surgery. Adequate drainage is indicated. Early the problem is one of combating the shock. This requires large quantities of plasma, whole blood, electrolytes, and fluids. The mortality rate is high, and in some sets of statistics it runs up to 65 per cent. In addition to the foregoing treatment, penicillin and streptomycin are given in large doses so that secondary infection may be minimized. A perforated peptic ulcer demands immediate operation, with closure of the perforation, because the chemical peritonitis is rapidly converted (in eight to twelve hours) into a bacterial peritonitis, with a very serious prognosis. Some believe that it is a bacterial peritonitis from the start. Clinically, it has been found that no drainage is necessary if the ulcer is closed within the first eight to twelve hours. If seen after that period, dependent drainage is indicated.

Peritonitis from fatty necrosis is not an emergency. The fat necrosis causes small nodules of soap to form, but these do no harm. If the diagnosis is uncertain, the surgeon will perform an exploratory operation. Should this condition be encountered, he may drain the gall bladder and the lesser peritoneal cavity. (See Chapter 22.)

Tumors and Cysts in the Omentum and Mesentery

Tumors are usually secondary to carcinoma of the stomach, colon, or pelvic organs. Cysts are often congenital and may be diagnosed by the fact that they present a movable tumor mass which is tympanic, due to the fact that cysts are usually in the mesentery, and therefore the bowel will be anterior to them.

Tuberculous peritonitis is often secondary to tuberculosis elsewhere and usually originates in the Fallopian tubes of the female or the appendix in the male. The exudative type is of slow evolution and is seen in young people, with the formation of excessive peritoneal fluid (ascites). The peritoneum is studded with thousands of small grayish-white tubercules. Simple laparotomy is often curative. Should the tubes or appendix be involved, they are removed. The proliferative type (dry) presents areas of caseation and results in fistulous formations if molested. (See Chapter 8.)

Gonorrheal peritonitis (see Chapter 22) is secondary to gonorrheal salpingitis and is rarely more than a pelvic peritonitis. The treatment consists of rest in bed, hot douches, heat to the abdomen, and large doses of penicillin and sulfadiazine. Surgery is withheld unless an abscess develops in the cul-de-sac, in which case it is drained through the vagina. Sometimes a chronic tubo-ovarian abscess must be removed.

Chemical peritonitis may be caused by a perforated peptic ulcer, which permits the hydrochloric acid of the stomach to irritate the peritoneum (this is discussed later in this chapter), or by acute hemorrhagic pancreatitis, in which activated trypsin causes a necrosis of the pancreas and steapsin (which needs no activation) is poured forth and digests the fat, causing fatty necrosis to occur (see Chapter 22).

A third type of chemical peritonitis is that produced by bile. Free bile in the peritoneal cavity may produce serious effects because of: (1) The toxic action of one or more of the products present in bile upon the tissues. This is probably due to the fact that bile salts make the peritoneum less resistant to infection. In clinical practice it is rare to find a bile peritonitis which has not become infected, although bile itself as found in the gall bladder is usually sterile. (2) The infection which is carried into the peritoneal cavity by the bile or subsequently developing through contamination. (3) The production of a condition like surgical shock, caused by the outpouring of large amounts of plasma into the abdomen through the permeable dilated capillaries and venules. The same effect may be produced by concentrated glucose introduced into the peritoneal cavity. Here the effect is one of an increase in the osmotic pressure within the peritoneal cavity, whereas in bile the effect is more of the nature of an inflammation with exudation. The result, however, is the same, and the picture is very much like that which occurs when shock is produced by other causes.

Clinically bile peritonitis does not often produce the shocklike picture described. In a patient who has recently been operated upon for gall bladder disease or in one who has had an attack of acute cholecystitis, any sudden shocklike picture should be interpreted as a large perforation. It is probably true that it takes a large sudden outpouring of bile to produce the syndrome. The picture may resemble a large perforated peptic ulcer with outpouring of gastric content, or a ruptured

palpated. A very careful examination of the female genital tract in elderly women is always indicated; also, careful examination of the bladder, ureters, and the kidneys.

Benign growths may be palpated at times, but often this is difficult. We have seen recently one patient in whom a lipoma protruded through the femoral canal. This was diagnosed as a femoral hernia and when the surgeon operated, he removed the small portion of the lipoma and found no hernia. This patient was referred to our service and upon exploration this was found to be a retroperitoneal lipoma which weighed eleven pounds. The man's symptoms were not only those of pressure on the femoral vein, but gastrointestinal pains with great discomfort as well.

There may be intestinal obstruction symptoms or peritoneal irritation with exudation or great ascites in the disseminated and malignant types of neoplasms. Due to the low-grade inflammation, adhesions form, giving bizarre symptoms and signs.

If free fluid is present, this should be studied carefully for (1) cells, inflammatory or neoplastic, (2) culture, (3) guinea pig inoculation, (4) direct smear, (5) protein content, which helps distinguish between transudates and exudates. In detecting tumors the fluid is centrifuged and a "button" is made which is examined after staining.

The treatment depends upon the condition which is found. Obviously, extensive secondary carcinomas defy extirpation. Mucocele of the appendix requires appendectomy, and the stump should be turned in carefully with two purse-string sutures, because sometimes the base of the appendix is involved. Certainly, it should not be ligated and left open in the presence of a mucocele. Some have stated that if the primary source is extirpated, the secondary implantation may be devitalized and thereby undergo regression. This has not been our experience. In cystadenocarcinoma of the ovary, even when the ovary is removed intact and before metastases are grossly apparent, the danger of secondary invasion of the peritoneal cavity is always present. However, the primary growths should be removed if this is feasible, especially in the absence of metastases. In pseudomyxoma peritonei the gelatinous material is scooped out of the abdomen and washed out as much as possible. This, of course, is only palliative and usually it does recur.

X-ray treatment is indicated in endothelioma and pseudomyxoma peritonei, although its effect is questionable. In small round-cell sarcoma or in lymphosarcoma, x-ray is beneficial. It is worthy of trial not only from the standpoint of its therapeutic effect, but also sometimes it aids in the diagnosis of the lesion by causing a prompt regression of the large growths.

Retroperitoneal Cysts.—Retroperitoneal cysts are not uncommon. The following is a classification which is fairly inclusive and which takes in most of the cysts that would ordinarily be encountered:

1. Cysts of urogenital origin. This includes cysts of the ureter, duplications of the ureter, perinephric cysts, renal cysts. Most of the fetal-renal elements may be found in various types of cysts. Some of

Neoplasms of the peritoneum may be primary or secondary, benign or malignant. Primary tumors are usually retroperitoneal, whereas secondary growths are ordinarily found within the peritoneal cavity. Benign primary tumors include lipoma, fibroma, neurofibroma, lymphangioma, hemangioma, myxoma, leiomyoma (usually in the omentum), ganglioneuroma, angioendothelioma, and various types of cysts which will be discussed later.

Malignant primary neoplasms are unusual and include sarcoma, fibrosarcoma, adenosarcoma, renal cell carcinoma, epithelioma, teratoma, lymphoma, neuroblastoma, endothelioma, or mesothelioma and undifferentiated neoplasms. More common are the malignant secondary neoplasms which may originate anywhere in the body but usually arise in the organs which are partially or completely covered by peritoneum. Therefore, one thinks of the gastrointestinal tract, pancreas, kidney, adrenal, uterus, and urinary bladder first, although carcinoma of the breast commonly metastasizes to the peritoneum. A rarer form of peritoneal neoplasm is known as pseudomyxoma peritonei (Pean's disease). The cause of this condition is obscure, although it has been known since 1842. It is associated with mucoceles, pseudomucinous cysts, or mucoid carcinomas anywhere in the abdomen. Usually, however, the appendix or ovary is the primary site. Not infrequently it follows a proliferating papillary cystadenoma of the ovary. These papilliferous growths are scattered throughout the abdominal cavity and constitute one of the most common types of secondary carcinoma of the peritoneum. The papillary cystadenocarcinomas infiltrate the omentum and mesentery and spread diffusely over the peritoneum and there forms cysts or pours out into the abdominal cavity a large quantity of gelatinous mucous material. It must be said, therefore, that this constitutes one of the forms of pseudomyxoma peritonei. However, a similar condition grossly may be produced by a secondary invasion of a mucoid carcinoma from other points of origin. Rupture of cysts containing mucin or mucoid material may cause the production of considerable amounts of this substance within the peritoneal cavity.

The diagnosis of peritoneal neoplasms may be difficult. This is particularly true of a generalized carcinomatosis of the abdomen, strange as this statement may sound. We have time and again seen patients with primary carcinoma of the ovaries with metastases through the abdomen, carcinoma of the uterus, primary carcinoma of the omentum, or retroperitoneal carcinoma or sarcoma which extends into the abdomen in which all of the usual forms of investigation are normal. These would include gastrointestinal series, scout films of the abdomen, barium enemas, retrograde pylorography, cystograms, and careful x-ray examination of the bony framework. Cystoscopic and proctoscopic examination may reveal very little from which to make a diagnosis, and many of these unfortunate victims are branded as psychoneurotics. The surgeon should be very cautious in making a diagnosis in patients who have vague pain within the abdomen and in whom various masses can be

primitive cell which shows epithelial elements in its wall. This type of cyst usually occurs in women and occupies a lateral position. (2) Those *derived from the mesodermal or lymphatic elements* and occur in any age group and in either sex.

The symptoms and signs of retroperitoneal cysts are discomfort, pressure, and the presence of a tumor mass. They are usually painless, but the enlargement of the abdomen and general discomfort cause the patient to seek medical attention. In addition, there may be anorexia and pain in the very large-sized growths. *The diagnosis is made by a process of elimination.* Sometimes this is extremely difficult. Pyelography, barium enema, and gastrointestinal studies may fail to reveal the diagnosis which may not be discovered until exploration is done. Cysts which arise in the adrenal, kidney, pancreas, or intestines must be thought of and ruled out in the differential diagnosis. They are, in a sense, retroperitoneal cysts.

The treatment is surgical, and in uncomplicated cysts the entire growth may be enucleated. However, usually they are related to the great vessels or the ureter or the intestine in such a way that their removal is not as simple as may at first be apparent. However, by careful dissection usually they may be removed. Lines of cleavage may be found if there has not been too much infection, and the cyst may be dissected loose. Not infrequently, due to the fact that the walls are thin, they may be ruptured and then enucleated. This would have no effect on the prognosis as a rule.

Intestinal Lipodystrophy

*An extremely rare condition of the mesentery is known as **intestinal lipodystrophy*** or *Whipple's disease.* The pathological aspects of this condition include changes in the mesenteric portion of the small bowel and its mesentery. The latter is thickened, yellow, and hard. The lymph nodes are enlarged and firm, and there are dilations of the lymph sinuses The lacteal vessels may be dilated enough to be seen grossly, indicating interference with lymph return and accounting for the chylous ascites which sometimes occurs. The mucosa of the jejunum and ileum is either normal in appearance or swollen and flecked with deposits of yellowish-white lipoid. In some cases fibrous pericarditis is present. Microscopic examinations show foam cells, extracellular and intracellular fat deposits, and foreign body giant cells, together with fibrosis and lymphocytic infiltration. The cause of this condition is entirely unknown, although Whipple believed that the fat in itself holds some abnormal or toxic substance. Another very popular theory as to its causation is the presence of fat necrosis, and this condition is related to the lipodystrophies that are seen elsewhere in the body.

The clinical picture is that of a patient who seems to be obese and yet seems to have vague masses within the abdomen that can be palpated. There is indigestion, gaseous distention, diarrhea, loss of weight,

these may have tubules and glomeruli in the wall and a ureterlike tubular structure. Some will have renal elements which are difficult to recognize and may even be found in the descending mesocolon. The cysts and, for that matter, solid neoplasms of the retroperitoneal space in relation to the adrenal, kidney, broad ligament, spermatic cord, epididymus, and possibly the testicle, have their origin in the wolffian body remnants. In addition to cysts that are in relation to the wolffian body are those that arise from cells of the genital ridge which lies just lateral to the wolffian body. Cases have been repored of ovarian cysts which lie to the outer side of the colon.

2. Teratomas and dermoid cysts. These, in our experience, have not been uncommon. In fact, retroperitoneal teratomas have been about as common as all of the other retroperitoneal tumors together. These include dermoid cysts and teratomas as well. They are frequently found in close association with the sacrococcygeal teratomas.

3. Lymphatic cysts. Cystic lymphomas have been described in Chapter 18. We have encountered many of these. Cystic hygromas and axillary and inguinal lymphatic cysts are reported in the literature in great numbers. Also cystic retroperitoneal lymphangiomas have been reported. It is now thought that the retroperitoneal lymphatic or mesenteric cysts are related to the cystic hygromas that are due to one of the primitive lymphatic sacs remaining in its primitive fashion. These cysts may have an endothelial lining, although it may be absent and the contents may be purulent or bloody, particularly in those which have been secondarily infected.

4. Jones describes a mesocolic type of cyst in which there is imperfect fusion of the layers of the peritoneum. It is conceivable that this can take place; however, it must be extremely rare. If it were found at all, it probably would be found between the layers of the ascending and descending mesocolon and rarely the transverse mesocolon.

5. Traumatic blood cysts are not difficult to understand, particularly following surgery on the uterus in which some of the endometrium has been inadvertently transplanted. Here there would be a blood cyst due to an endometriosis. Traumatic blood cysts imply trauma plus a hematoma with absorption of the hematoma and cyst formation.

6. Parasitic cysts, particularly the echinococcus cysts.

7. Developmental cysts in the fully formed kidney or pancreas or liver. These are really not retroperitoneal in the sense that we are describing retroperitoneal cysts. These belong to the organ in which the cyst is found.

8. The pseudopancreatic cyst which forms as a result of injury or diseased pancreas and results from a closure of the gastroepiploic foramen with an accumulation of fluid in the lesser peritoneal sac.

In this discussion it can be seen that generally there are two types of cysts: (1) Those which are derived from the ectodermal or perhaps the entodermal elements of the wolffian body or genital ridge, or a more

4. Neoplastic diseases with dissemination of neoplastic tissue over the peritoneal surface such as occurs in proliferating papillary cystadenocarcinoma of the ovary with dissemination, this to be distinguished from occlusion of the portal vein due to metastases in the liver
5. Rarely ascites may occur as a result of fibroma of the ovary and this may be accompanied by pleural effusion as well as by ascites as in Meigs' syndrome. (See Chapter 22.)

C. *Combinations*

Combinations of causes occur in which the obstructive factor and the changes in the osmotic pressure in the blood may play a role. This is commonly observed in late carcinoma where the neoplastic elements in the peritoneal cavity produce a local irritation, and, in addition, there may be cardiac impairment producing ascites from increase in hydrostatic pressure in the veins. The ascitic fluid varies greatly in color and consistency. Usually the fluid is clear and yellowish; in carcinoma it is blood tinged; in chylous ascites it is white or milky. In the young, ascites is most commonly associated with Banti's disease (portal hypertension) or with tuberculosis. In older individuals cirrhosis of the liver and carcinoma are the most common causes.

The treatment of ascites is medical or surgical. Medical treatment consists of the control of the primary cause if possible, and, in addition, the use of diuretics. The surgical treatment most frequently employed is that of paracentesis which may be repeatedly carried out (paracentesis peritonei). There have been attempts, however, to form a more permanent type of drainage of ascitic fluid from the peritoneal cavity such as subcutaneous channels made of glass or metal tubes, anastomosis of the peritoneum to the saphenous veins or the renal pelvis, the use of venous grafts from the peritoneal cavity to the subcutaneous space, cannulas inserted in the peritoneal cavity and brought to the outside, resection of the parietal peritoneum. Also methods have been devised to improve the collateral circulation such as the omentopexy of Talma, anastomosis of the sigmoidal veins to the saphenous veins; the splenic to the left renal vein; the superior mesenteric to the vena cava, or the portal vein to the inferior vena cava. Needless to say, surgery is indicated in those conditions which are due to neoplasms or in which there is great splenomegaly. For further discussion of ascites, see Chapter 22.

GASTROINTESTINAL CANAL

Embryology and Physiology

The mesenteron, or central portion of the alimentary canal, is formed from entoderm and consists at first of a simple tube which ends blindly anteriorly and

and general debility. There is a general tendency toward achlorhydria and fat intolerance. The diagnosis is usually made at operation. The prognosis is unfavorable. The treatment is entirely unsatisfactory and most of the patients die within several months to a year and a half. Surgery is of little avail and usually is done because the diagnosis is uncertain. The use of x-ray therapy is likewise not of much help.

Ascites

Fluid in the peritoneal cavity is known as ascites. This fluid may be a transudate or an exudate and may consist of plasma, serum, the products of exudation or chyle (chylous ascites). Ascites may be produced experimentally in the following ways:

1. Ligation of the common bile duct in dogs will produce ascites and this will increase after a high protein diet.
2. Massive saline infusions provided the kidney output is much less than the amount infused.
3. Constriction of the inferior vena cava above the liver by suture, metal bands, or cellophane bands.
4. Constriction of the pericardium especially around the right auricle by sutures or by bands.

Ascites cannot be produced by occlusion of the portal vein or the vena cava below the diaphragm. However, cirrhosis may be induced by the gradual occlusion of the portal vein and this, in turn, may give rise to at least temporary ascites.

The clinical causes of ascites may be listed under the following headings:

A. *General Causes*
   1. Increase in the hydrostatic pressure in the veins
      a. Cardiovascular disease, renal disease
      b. Constrictive pericarditis
      c. Mediastinal tumor with increase in venous pressure
   2. A decrease in the osmotic pressure
      a. Due to excessive amounts of intravenous fluids
      b. Starvation with a decrease in the osmotic pressure due to hypoproteinemia

B. *Local Causes*
   1. Increase in hydrostatic pressure of the veins due to hepatic disease, portal hypertension from thrombosis of the portal or splenic vein or Banti's disease and splenomegaly
   2. Increase in the hydrostatic pressure of the lymphatics due to new growth such as carcinoma and inflammation such as tuberculosis
   3. Inflammatory diseases such as tuberculous peritonitis or any form of chronic peritonitis

4. Neoplastic diseases with dissemination of neoplastic tissue over the peritoneal surface such as occurs in *proliferating papillary* cystadenocarcinoma of the ovary with dissemination, this to be distinguished from occlusion of the portal vein due to metastases in the liver
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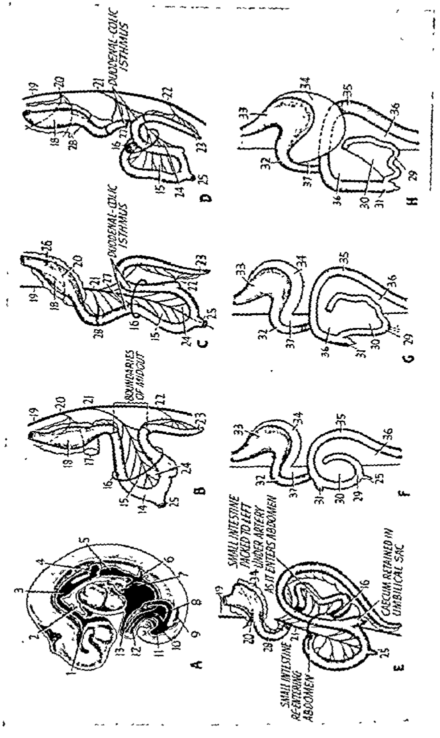
DUODENAL-COLIC ISTHMUS
DUODENAL-COLIC ISTHMUS
BOUNDARIES OF MIDGUT
SMALL INTESTINE PACKED TO LEFT UNDER ARTERY AS IT ENTERS ABDOMEN
CAECUM RETAINED IN UMBILICAL SAC
SMALL INTESTINE RE-ENTERING ABDOMEN
A
B
C
D
E
F
G
H

Fig. 271.—Diagram illustrating the extrusion, rotation and reinclusion of the midgut.

A. *About fourth-week embryo (5 mm.)*, showing the entodermal canal and its derivatives. (1) Rathke's pouch; (2) tongue, (3) laryngotracheal groove, (4) left lung, (5) stomach; (6) dorsal pancreas, (7) liver; (8) *allantois*, (9) *mesonephric* duct, (10) metanephron, (11) cloaca, (12) allantoic stalk; (13) yolk stalk

B. First stage of rotation, about the fifth week. Sagittal section showing the midgut in the process of extrusion (due to its rapid growth and the growth of the right lobe of the liver). (14) midgut, (15) prearterial mesentery, (16) umbilical orifice, (17) anterior mesogastrium; (18) foregut; (19) aorta, (20) celiac axis, (21) superior mesenteric artery, (22) inferior mesenteric artery, (23) hindgut, (24) postarterial mesentery, (25) vitelline duct and artery.

C. About seventh-week embryo, showing further extrusion of the midgut through the umbilical orifice (15) *prearterial mesentery*, (16) umbilical orifice; (18) foregut, (19) aorta (20) celiac axis, (21) superior mesenteric artery, (22) inferior mesenteric artery; (23) hindgut; (24) postarterial mesentery; (25) vitelline duct and artery, (26) great omentum (dorsal mesogastrium), (27) pressure here by left umbilical vein, (28) ventral mesogastrium.

D. End of extrusion, about ninth week, showing the rotation of the midgut in a counter-clockwise manner. (15) prearterial mesentery; (16) *umbilical orifice*, (18) *foregut*, (20) celiac axis; (21) superior mesenteric artery; (22) inferior mesenteric artery; (23) hindgut; (24) post arterial mesentery; (25) vitelline duct and artery, (27) pressure here by left umbilical vein, (28) *ventral mesogastrium*.

E. Tenth-to-eleventh-week embryo showing the progress of rotation coincident with the return of the midgut to the abdomen. (16) umbilical orifice, (19) aorta; (20) celiac axis, (21) superior mesenteric artery, (25) vitelline duct, (28) ventral mesogastrium, (34) great omentum.

F. Completion of the stage shown in *E*, and further migration of the cecum and colon to the right side (25) vitelline duct; (29) small intestine; (30) mesentery, (31) cecum, (32) duodenum (33) stomach; (34) great omentum, (35) colon, (36) mesocolon, (37) mesoduodenum.

G. Continued migration and descent of the cecum to *the normal position*. (29) *small intestine*, (30) mesentery, (31) cecum; (32) duodenum, (33) stomach, (34) great omentum, (35) colon, (36) mesocolon; (37) mesoduodenum.

H. Completed migration and fusion of the mesentery begun (25) colon, (29) small intestine; (30) mesentery, (31) cecum, (32) duodenum; (33) stomach; (34) great omentum, (36) mesocolon; (37) mesoduodenum.

(From Berman. Congenital Anomalies of the Midgut, Internat Clin, Vol. iv, series 47, 1937. Redrawn from Prentiss, C. W., A Laboratory Manual and Textbook of Embryology, W. B. Saunders Company, and Fraser, John: Surgery of Childhood, William Wood & Co.)

posteriorly. This tube represents only the mucous membrane. Later it becomes enveloped in a layer of mesoderm, which differentiates into two portions, the outer forming the peritoneal covering and the inner forming the muscle and connective tissue elements. In embryos of thirty to sixty days, the epithelium proliferate rapidly, and the alimentary canal down to the ileocecal may be obliterated by the excess of epithelium (solid stage). Soon vacuoles appear, then coalesce, re-establishing the lumen by the twelfth week. These same phenomena are said to occur in the esophagus, stomach, and colon to a much lesser degree. Should a septum persist, an atresia results, and if partially open stenosis remains, an invagination of ectoderm takes place at the two ends, anteriorly forming the stomadeum, which later becomes the mouth, and posteriorly, the proctodeum, which becomes the anal orifice. As the embryo develops, this tube becomes slightly dilated at the levels of the future stomach and colon. Due to the rapid growth of the liver and gut, there is not enough room for its further development, and at about the fifth week the intestine is extruded through the umbilical opening. Attached to the gut is a duct (the omphalomesenteric duct or vittelined duct) which connects the yolk sac with the midgut, and at its intestinal attachment a small pouch may be left (Meckel's diverticulum) which persists in about 2 per cent of adults, or the duct may fail to close, forming an umbilical fistula. Between the fifth and tenth week the abdominal cavity is large enough to accommodate the intestines and they re-enter, first, the small intestine, then the cecum (to the upper left quadrant, with the ileum entering from the right to left), then the colon. The cecum then migrates to the right upper quadrant and finally to its normal position in the right ileac fossa.

The foregut gives rise to the upper portion of the alimentary canal, part of the oral cavity, the pharynx and its derivatives, the esophagus, the stomach, and the first portion of the duodenum (down to the duodenal papilla and from the duodenum, the liver and pancreas). It is supplied by blood from the celiac axis, and its function is chiefly digestive. It, indeed, is the chemical laboratory of the alimentary canal. The chief digestive fluid of the foregut is the gastric juice, composed of rennin, which coagulates or curdles milk, and hydrochloric acid and pepsin for protein digestion; also inorganic salts, histamine, lipase (traces), and the antianemic factor of Castle.

There are approximately 35,000,000 gastric glands in the fundus and body of the stomach. The chief cells in the neck of the glands secrete mucin, as do the pyloric glands, whereas those in the body of the gland (zymogenic cells) secrete pepsin or its precursor; parietal cells in the gland secrete the hydrochloric acid. Glands about the pylorus and esophagus and in the cardiac end of the stomach secrete chiefly mucin. Gastric lipase is a fat-splitting enzyme which acts only in an acid medium.

If the stomach content has a free HCl value below 20 after a test meal, the condition is called hypochlorhydria, or subacidity. Complete absence of free HCl is called achlorhydria, or anacidity (present in 4 to 10 per cent of normal adults). Complete absence of acid and pepsin is referred to as achylia gastrica. Anacidity is found in pernicious anemia, carcinoma, and chronic gastritis. Hypochlorhydria may be found normally and also in gall bladder disease, Addison's disease, and sprue. Hyperchlorhydria, or hyperacidity, is the condition in which the free acid is above normal (60 to 90), remaining high after the first hour following a test meal. This is not due to the secretion of an excessively acid juice (the maximum acidity is 0.4 to 0.5 per cent HCl). It is due to a hypersecretion (secretion of too much juice) or to a failure of neutralization. This is seen in peptic ulcer, especially if associated with pyloric obstruction.

The stomach absorbs alcohol, some glucose, and water but almost nothing else. It cannot be regarded as an absorptive organ. Mucin secreted by the pyloric and Brunner's glands (in the pyloric antrum and pars superior duodeni) is present to protect the lining of the stomach and duodenum against the corrosive action of the hydrochloric acid.

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Vagal stimulation which is weak produces mucus which is alkaline; when strong, it is acid. Brunner's glands are activated by vagal stimulation. Vagotomy decreases mucus production. Stimulation of the sympathetics (splanchnics) causes mucus production.

Chemical stimulation. High acid usually calls forth more mucus even in atropinized animals. Histamine stimulates parietal cells but inhibits the production of pepsin and mucus. Adrenaline simulates sympathetic stimulation in that it increases the spontaneous secretion of alkaline or neutral mucus. Secretin stimulates Brunner's gland. Acetylcholine produces a secretion of very thick mucous fluid which possesses a high peptic power but is only slightly acid. When histamin and acetylcholine are used, a secretion richer in pepsin and mucus and lower in acidity is produced than when histamin alone is employed.

Local mechanical irritation provokes the secretion of mucus.

Gastric mucus serves to lower gastric acidity, inhibits pepsin, and acts as a mechanical protection for the mucous membrane when irritated; however, the lowering of gastric acidity by alkaline mucus is most effective when the secretion of gastric juice is at low ebb. This is accomplished by neutralization and adsorption, and therefore it is most prominent at the beginning of a meal (cephalic phase) and at the end of a meal when much of the acid has been used in the digestion of a meal. Thus it serves to protect at such times when there is no food to take up the hydrochloric acid and would have its greatest protective influence at the beginning and end of a meal, between meals, and at night.

The normal rate of secretion varies between 30 and 117 c.c. per hour, and it is more or less continuous. This has been called the interdigestive secretion and is said to be an important factor in the causation of ulcer, particularly during the night when the stomach is empty. The total volume of gastric juice is 2 to 3 liters per day (interdigestive and digestive juices). (See Chapter 11.)

The digestive secretion is divided into three phases: (1) The psychic (cephalic). This phase is extremely important and gives rise to a strong psychic juice. Secretory fibers for the gastric glands are found in the vagus and splanchnic nerves. Insulin provokes gastric secretion by the hypoglycemic stimulation of the vagal center. This test is now used to determine whether the vagi have been completely severed after vagotomy. The thought, sight, smell, or taste of food stimulates psychic juice. Resentment, hostility, aggressivenes, and anxiety produce hypersecretion and hypermobility and increased congestion of the gastric mucosa—even superficial ulceration (Wolf and Wolff); Sadness, discouragement, and self reproach produce hyposecretion

posteriorly. This tube represents only the mucous membrane. Later it becomes enveloped in a layer of mesoderm, which differentiates into two portions, the outer forming the peritoneal covering and the inner forming the muscle and connective tissue elements. In embryos of thirty to sixty days, the epithelium proliferate rapidly, and the alimentary canal down to the ileocecal may be obliterated by the excess of epithelium (solid stage). Soon vacuoles appear, then coalesce, re-establishing the lumen by the twelfth week. These same phenomena are said to occur in the esophagus, stomach, and colon to a much lesser degree. Should a septum persist, an atresia results, and if partially open stenosis remains, an invagination of ectoderm takes place at the two ends, anteriorly forming the stomadeum, which later becomes the mouth, and posteriorly, the proctodeum, which becomes the anal orifice. As the embryo develops, this tube becomes slightly dilated at the levels of the future stomach and colon. Due to the rapid growth of the liver and gut, there is not enough room for its further development, and at about the fifth week the intestine is extruded through the umbilical opening. Attached to the gut is a duct (the omphalomesenteric duct or vittelined duct) which connects the yolk sac with the midgut, and at its intestinal attachment a small pouch may be left (Meckel's diverticulum) which persists in about 2 per cent of adults, or the duct may fail to close, forming an umbilical fistula. Between the fifth and tenth week the abdominal cavity is large enough to accommodate the intestines and they re-enter, first, the small intestine, then the cecum (to the upper left quadrant, with the ileum entering from the right to left), then the colon. The cecum then migrates to the right upper quadrant and finally to its normal position in the right ileac fossa.

The foregut gives rise to the upper portion of the alimentary canal, part of the oral cavity, the pharynx and its derivatives, the esophagus, the stomach, and the first portion of the duodenum (down to the duodenal papilla and from the duodenum, the liver and pancreas). It is supplied by blood from the celiac axis, and its function is chiefly digestive. It, indeed, is the chemical laboratory of the alimentary canal. The chief digestive fluid of the foregut is the gastric juice, composed of rennin, which coagulates or curdles milk, and hydrochloric acid and pepsin for protein digestion; also inorganic salts, histamine, lipase (traces), and the antianemic factor of Castle.

There are approximately 35,000,000 gastric glands in the fundus and body of the stomach. The chief cells in the neck of the glands secrete mucin, as do the pyloric glands, whereas those in the body of the gland (zymogenic cells) secrete pepsin or its precursor; parietal cells in the gland secrete the hydrochloric acid. Glands about the pylorus and esophagus and in the cardiac end of the stomach secrete chiefly mucin. Gastric lipase is a fat-splitting enzyme which acts only in an acid medium.

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and pallor of the gastric mucosa. (2) Gastric phase stimulated by (a) the mechanical distention of the stomach and (b) chemical excitatory stimuli. The latter may be in the food or may arise as products of digestion; they may act directly as secretogogues or indirectly through the liberation of a gastric hormone. Histamine is the best known and most effective secretory chemical stimulus. Others are peptones, meat, extracts, alcohol, liver extracts, and pyloric mucosa (Kamarov). (3) Intestinal phase which is provoked by secretogogues in the intestines. Serious distention inhibits gastric secretion; injury to intestinal mucus stimulates it, probably due to histamine release.

Gastric secretion is inhibited by (1) Chemical or hormonal factors: (a) Acid in the stomach or intestine and ulcer which has not been produced in the experimental animal by acid alone; we have shown that acid does stimulate the mucous cells and there is an increased amount of mucin; (b) enterogastrone which is released by the presence of fat in the intestine; (c) dextrose which may inhibit gastric secretion, particularly in the hypoglycemic state; (d) an inhibitory substance found in the urine (urogastrone). (2) Nervous inhibitory factors: (a) through the vagi and splanchnic; mental states inhibit gastric secretion; (b) distention of the intestine. Gastric juice secretion is affected by many factors not as yet fully understood such as internal secretion (thyroid and parathyroid) and vitamins, especially B complex. In hyperparathyroidism and hypercalcemia gastric secretion is inhibited, whereas in hypocalcemia it is increased. Deficiency of the vitamins A and B decreases secretion as do other food and water and salt deficiencies. Tobacco does not stimulate secretion; morphine does. Vagotomy decreases secretion but has no effect on the secretory response of the stomach to histamine or caffeine; however, it does abolish the stimulating effect of insulin hypoglycemia. X-rays, fever, anemia, and anoxemia decrease secretion.

As digestion proceeds, psychic, gastric, and intestinal phases of secretion cause the rise and fall of the volume of gastric secretion. Then, too, such factors as enterogastrone, acid inhibition, and gastric emptying time affect the volume. The acid volume is affected by (1) food which combines with acid and ''sops'' it up, (2) alkaline secretions of the stomach (mucus and mucoid secretion) and bile and pancreatic juice, (3) and the products of peptic digestion which inhibit secretion.

Motor Activity of the Stomach.—The metabolic requirements of the body are made known to man by the sensation of hunger. This sensation in turn is probably due to hunger contractions of the stomach. Animals appear to experience hunger after gastrectomy or denervation. This shows that in addition to stomach contractions a central mechanism may play a role.

As food enters the stomach, it is held in the fundus and body (the hopper) where it undergoes little changes except some liquefaction. Periodically some of the food is forced into the pylorus (the grinder), where it is mixed and ground, and passed toward the sphincter by peristaltic waves, starting near the incisura and cardia. Fluids usually begin to leave the stomach within a few minutes. Solids take a longer time. If the material is irritating to the duodenum, still more time is required.

Gastric evacuation occurs chiefly as a result of antral activity, or the difference in pressure between the antrum and bulb rather than the activity of the pyloric sphincter. If the antral wave is so strong as to occlude the sphincter completely, most of the material returns to the body of the stomach. Peristaltic waves begin in the incisura during most of the digestion, but as the stomach becomes empty, the waves originate higher. The pylorus responds to approaching waves of peristalsis much as does the adjacent part of the pars pylorica, and the relaxation of the pylorus alone is not followed by the passage of food. This takes place only when the pylorus and the duodenum are relaxed at the same time. Stretching of the stomach hastens evacuation. The antrum (mostly) and the sphincter and bulb (to some extent) are inhibited by great distention of the duodenum, or by fats, hydrochloric acid, protein-split products,

sugars, and intravenous hypertonic solutions. Inhibition of the region of the sphincter results from the enterogastric reflex and enterogastrone.

Gastric motility tends to be inhibited by vagotomy and augmented by splanchnicectomy. On theoretical grounds, excessive activity of the sympathetics might lead to spasm of the cardia, atony of the fundus and body, spasms of the pyloric sphincter, and a decreased motility of the intestines. No changes in secretion of gastric juice will result, but there should be local and general vasoconstriction. Afferent sensory nerve fibers run with the sympathetics and, therefore, if they are divided, there should result atony or relaxation of the cardia and pylorus and increase in tonus and motility of the stomach; in addition, partial anesthesia.

The vagus mechanism is theoretically antagonistic to the sympathetics, and if there is excessive activity of the efferent vagus fibers, there should be a relaxation of the cardia and pylorus, increased motility and tonus of the stomach, and an increased secretion of gastric juice. Afferent pain fibers probably do not run in the vagus. Division of the vagus should cause spasm of the cardia and pylorus, atony of the stomach, decreased secretion of gastric juice, and no anesthesia.

In addition to these extrinsic nervous mechanisms, there is an intrinsic or local automatism throughout the gastrointestinal tract. Experiments by Cannon and others have shown that complete denervation does not prevent normal function, and moreover that new fibers soon find their way into the denervated organ from many adjacent sources. If the entire autonomic nervous system is interrupted, the experimental animal loses its homeostatic adaptabilities for a while, then gradually regains them.

By nervous control through the sympathetics and parasympathetics (see Chapter 18) food is not only digested but also propelled by peristaltic waves into the intestines below. The entire gastrointestinal tract is laid down around the inner layer (mucosa). External to this is the muscularis mucosa; then the tough submucous coat, made so by its fibrous tissue; then the muscularis; and, externally, the serosa (visceral peritoneum). The secretory functions are carried out through gastric glands (in the stomach) and intestinal glands (in the intestines), aided by the pancreatic juice.

Mid-gut.—The mid gut gives rise to the intestine from the second portion of the duodenum to the middle of the transverse colon. It is nourished by the superior mesenteric artery and its function is chiefly absorptive. The small intestine is covered with villi—about 20 to 40 to the square millimeter. Each villus has a lymph vessel (lacteal), an arteriole, a capillary plexus, and several venules. Between the villi are the crypts of Lieberkuhn. The cells are columnar and may become transformed into goblet cells which secrete the protective mucus. There are four types of cells in the crypts: columnar and goblet cells, whose functions are protective; argentaffine cells, which may be endocrine elements or producers of intestinal ferments; and cells of Paneth, which probably supply the intestinal juice.

Intestinal Absorption.—Absorption takes place through the intestinal villi, of which there are about 5,000,000 in the human intestine. Amino acids and glucose are absorbed by the capillaries Of the digested fat, 60 per cent passes into the lacteals; the fate of the remaining 40 per cent is uncertain.

The physiological causes of intestinal absorption have been explained in different ways:

1. Differences in concentrations and therefore of diffusion pressures between crystalloids in the blood and in the intestinal lumen.

2. Increased hydrostatic pressure in the intestine due to peristaltic movements. (In intestinal obstruction this pressure may cause absorption by forcing fluid directly through the distended bowel wall into the peritoneal cavity.)

3. The colloid osmotic pressure in the capillaries of the villus (caused by the plasma proteins) which is two to three times greater than the hydrostatic pressure in these vessels and so brings about absorption.

In the mid-gut the partially digested meal is changed further by the pancreatic juice poured into the duodenum at the ampulla of Vater (through the pancreatic and accessory pancreatic ducts of Wirsung and Santorini) and contains trypsin for protein digestion, amylase for carbohydrates, and lipase for fats.

There is also some rennin in pancreatic juice, some maltase, and possibly erepsin. The secretion of pancreatic juice is both under hormonal (secretin, prosecretin) and nervous (vagus) control. Pancreatic juice is alkaline in reaction and contains electrolytes essential to life. Total loss of the juice by fistula results in death due to dehydration and loss of electrolytes. In experimental animals life may be prolonged by Ringer's solution and normal saline for a few weeks.

Bile from the common bile duct also enters the duodenum at the ampulla and aids in the digestion of fats and perhaps stimulates the motor function of the intestines. The digestive ferments in the intestinal juices are (1) various peptidases (erepsin), (2) sucrose, maltose, and lactose for the digestion of the disaccharides cane sugar, malt sugar, and milk sugar, (3) lipase, and (4) some amylase.

Hind-gut.—The hind-gut gives rise to the remainder of the colon and to the rectum but not to the anus. It is nourished by the inferior mesenteric artery, and its function is chiefly excretory, although absorption of water and salts occurs.

At birth only the terminal part of the pelvic colon lies in the pelvis. This is due to the small size of the pelvic cavity. Furthermore, the iliac colon lies in the left iliac region, but the sigmoid flexure (pelvic colon) usually lies on the right side and passes over the right portion of the brim to enter the pelvis. The small pelvis in the linear type adult apparently does not prevent the complete descent of the pelvic colon commonly seen in the lateral type.

Anatomical and Physiological Considerations of the Large Intestine

The large intestine is equal to about one-fifth of the entire intestinal canal and measures five to five and one-half feet. Its breadth is greatest at the cecum, and from this, with the exception of a dilatation at the rectum, it gradually decreases to the anus. At the cecum it measures, when distended about three inches in diameter; beyond this it gradually diminishes and measures only one and one half inches, or less, in the descending, iliac, and pelvic divisions of the colon. The iliac colon has no mesentery, whereas the pelvic colon has a well developed one. This permits a wide range of movement. It usually crosses the pelvis from right to left, then bends backward and returns along the posterior wall of the pelvis to the median line. The layers of the large bowel are like those of the small; namely, mucosa, muscularis, submucosa, circular muscle, longitudinal muscle, and serosa. The large intestine, with the exception of the rectum and vermiform process, may be easily distinguished by the three longitudinal bands, or taeniae coli, and the appendices epiploicae. The longitudinal fibers of the muscular coat do not form a complete layer continuous all around the bowel but are broken up into these three bands which are about one fourth inch (6 mm.) wide. They begin at the base of the appendix and extend along the surface of the gut at nearly equal distances until the rectum is reached, where they form a continuous layer of longitudinal muscle fibers. Since the taeniae are one-sixth shorter than the intestine to which they belong, the bowel is thrown into sacculations.

Three rows of saccules are thus produced along the length of the bowel between the longitudinal bands. If the taeniae are dissected off, or their contractile power is reduced under anesthesia or post mortem, the sacculation is largely lost. On the inside of the bowel the saccules give rise to pouches (haustra) separated by crescentic folds (plicae semilunaris coli) which correspond to the creases on the outside separating the saccules.

The taeniae lie on the anterior, posterolateral, and posteromedial side of the gut. The appendices epiploicae lie chiefly on either side of the anterior longitudinal band. Here diverticula are frequently encountered. On the transverse colon the arrangement

appears differently, but if it is turned up on the abdomen, the bands are in the same position. However, as seen within the abdomen, the anterior taenia becomes the posteroinferior (taenia libera) and the posterolateral becomes the anterior (taenia omentalis), whereas the posteromedial becomes the superior (taenia mesocolica). The posterolateral taenia of the iliac colon passes below to the front of the pelvic colon and rectum and unites with the anterior taenia to form a broad band which occupies nearly the whole width of the bowel. The posteromedial taenia spreads out in a similar manner on the back, so that the lower portion of the pelvic colon has almost a complete longitudinal layer, except a narrow margin on each side. Here the circular muscles come to the surface, and sacculations, although small, are present. These disappear as the rectum is approached, and the longitudinal muscles are thicker.

The blood vessels of the large bowel enter from the mesentery along the mesenteric side of the lateral and medial posterior taeniae and also some small vessels between them. Since the longitudinal muscle is incomplete, the vessels lie rather superficially between the posterior and anterior longitudinal bands beneath the serosa. This accounts for the enormous distention which is possible in the large intestine without complete interference of the blood supply, as compared with the relatively small amount of distention tolerated in the small bowel where the vessels are covered by both circular and longitudinal muscles.

Diverticula are frequently found where the blood and lymph vessels enter or leave the bowel, for it is here that the circular muscle is defective and the area of least resistance is created. Since the veins are larger than the arteries and are easily distended by passive congestion, this opening rather than the arterial is probably at fault at the onset, although there is no proof of this.

Motor Activity of Large and Small Intestines.—The large bowel is innervated by the sympathetics and parasympathetics (craniosacrals). The former is inhibitory and the latter stimulative, while the sphincters (ileocolic, internal, and external anal) are contrarily innervated; that is, the motor nerve to the sphincters is through the sympathetics, and the parasympathetics are inhibitory. Therefore, stimulation of the parasympathetics increases bowel tone and causes relaxation of the sphincters, whereas stimulation of the sympathetics inhibits intestinal activity and causes a contraction of sphincters (reciprocal innervation or contrary innervation), although the external anal sphincter is also under voluntary control.

Due to this dual mechanism and also to the rhythmical property of intestinal muscle itself, certain movements are seen in the large bowel. There is little movement in the cecum and the fecal mass is propelled by (a) passive overflowing of the cecum and (b) slow ill-defined contractions. Although some antiperistaltic waves have been seen in lower animals, this has not been observed in man.

The rest of the large bowel, unlike the small, does not show antiperistaltic, segmenting, or to-and-fro pendulum like movements. Even peristalsis is ill-defined. There is contraction of the circular muscle showing the sacculations and, in the transverse colon, some weak movements and alternate shortenings and elongations. By far the most important motor action of the large bowel is the mass peristalsis which sweeps the contents for some distance. This corresponds to the "rush" wave of the small intestine. It is said to occur not more than two to three times in twenty-four hours, and the subject is normally unaware of it. Sometimes it is initiated after eating (gastrocolic reflex) and, no doubt, psychic influences affect this.

The wave usually begins in the hepatic flexure and the colon loses its haustral markings. The fecal mass is moved into the pelvic colon, which acts as a storehouse, and then the haustral markings reappear. The ascending, transverse, and descending colon are usually empty, except when transferring feces, and the pelvic colon fills from below, upward. It is evacuated through the rectum and anus by defecation. The rectum is also empty except preceding and during the act of defecation.

When the fecal mass fills and distends the rectum between 40 and 50 mm. Hg, the defecation reflex occurs. This is as follows:

1. Strong peristaltic contraction of the colon.

2. Shortening of longitudinal bands which are indirectly fixed to the rectococcygeus muscle.

3. Relaxation of sphincters.

4. Voluntary contraction of abdominal muscles and fixation of diaphragm in inspiration, causing a rise in intra-abdominal pressure. This depresses the ascending, transverse, and splenic flexure of the colon. The fixed cecum becomes globular, and the intrarectal pressure, which is normally 20 mm. Hg, may rise to 100 to 200 mm. Hg during straining. The levatores ani, transversi perinei, and coccygeus muscles prevent prolapse, and the former actually pull against the descending force.

Leading from the intestine are lymphatics and lymph nodes, which lie in the mesentery, close to the arteries and veins. The portal vein carries the absorbed food products to the liver to be stored as glycogen or to be detoxified, whereas the lymphatics (lacteals) carry their emulsified fat to the blood by way of the thoracic duct. The situation of lymph nodes is important to the surgeon because of their frequent involvement in carcinoma.

The entire gastrointestinal canal is in a state of continual motion (peristalsis), carried on by the muscular layers of the bowel, with stronger waves at the upper and weaker at the lower end of the small bowel. In the small intestine there are waves producing a to-and-fro churning action and "rush" waves going straight downward; there are reverse waves in the ascending colon, forward waves in the transverse and descending colon, and strong waves in the sigmoid, which are felt as a desire to defecate.

Many other conditions affect the peristaltic movements and the progress of the fecal stream to the small and large intestine. The valvula coli (ileocecal valve) has been the subject of much study, and many theories have been advanced as to its structure and function. These are (1) that the ileum is separated from the cecum by sphincter muscle and (2) that the cecum is separated from the ileum by a valve. Probably both of these theories are correct. The ileocecal valve attains development late in fetal life and often does not develop completely until after birth. Consequently, there is a great variation in its structure and also in its function as a result of its structural differences. Perhaps the adequacy or inadequacy of the ileocecal valve function is best explained on the basis of arrested development. As a rule, when fully developed, the valve is represented by two transverse folds lying above and below its orifice and constituting the two segments of the valve. These are known as labii and resemble a small intussusception. These labii are formed of an infolding of all coats of the gut except the peritoneum and the longitudinal muscle layers and are covered by the mucosa of the ileum and cecum on their respective surfaces. The two valve segments are elevated and slightly approximated when the cecum distends. The more distended the cecum becomes, the tighter will be this approximation. The cecum must become distended for the valve to function. The valve is very strong and is almost as thick as the intestinal wall. Therefore, it would be able to withstand more pressure than the cecal wall itself. The importance of the ileocecal valve is seen in the distention of the large intestine caused by obstruction distal to the ileocecal valve. The use of the Levine tube or the Miller-Abbott tube, as is well known, will decompress the small intestine but not beyond the ileocecal valve, where decompression must be done by cecostomy or transverse colostomy. However, in children where the valve is not always fully developed, this does not necessarily hold true. A Miller Abbott tube will very often decompress the large bowel as well as the small intestine. A good rule to follow, then, is that in the case of obstruction below the ileocecal valve, some form of decompression other than the Miller-Abbott tube should be used in order to avoid the possibility of a perforation of the cecum. This is usually a cecostomy or transverse colostomy, depending on the site of large bowel obstruction.

Other practical observations concerning intestinal motility before and after operation and its relation to postoperative distention have been described. The contrary type of motility between the small and large bowel has been noted when the small bowel is vigorously contracting and the colon is inactive. Conversely, when the colon contracts, the small intestine appears to be inhibited. Those drugs including the opiates, physostigmine, Prostigmine methyl sulfate, and the derivatives which stimulate the motility of the small bowel appear to inhibit the motility of the colon. Posterior pituitary gland solutions and Pitressin produce powerful contraction of the colon but diminish the motility of the small bowel. In addition, Pitressin has a restrictive effect on smooth muscle and therefore is not used postoperatively because of the danger of coronary occlusion and other types of vascular occlusions which might occur within the abdomen or the extremities. Postoperative distention may be due to the action of morphine on the colon. The effects of heat and cold on the bowel are variable. It has been said that cold increases peristalsis and tonus of the stomach and bowel when applied externally and that cold causes a sharp rise in the gastric acidity. When applied internally by drinking ice water, the reverse effect is produced. Heat applied externally decreases tonus and peristalsis and when applied internally by drinking hot water, increases tonus and peristalsis. This has been discussed previously. (See Chapter 5.) However, these results are not invariable because the state of tonus and motility of the gastrointestinal canal is constantly varying, and the effect of cold on gastric motility may be dependent on the state of tonus at the time that the temperature has been lowered. Perhaps the comfort of the patient should determine whether or not hot or cold applications are best. However, there is enough experimental evidence to show that the effects of heat upon the blood supply to the bowel is that of dilation, and since it conceivably does tend to tone down peristalsis or activity, it would be useful in the treatment of an inflammatory disease of the abdominal cavity. Furthermore, usually the patient is more comfortable with heat than with cold, although after a while, cold so completely freezes the part that it becomes more or less insensitive to pain.

Gaseous Distention.—The causes of gaseous distention of the gastrointestinal tract has been the subject of long and arduous investigation. The gas in the intestine is there for the following reasons: (1) aerophagy or swallowing of air, (2) air sucking or air suction, (3) fermentation, and contrary to popular opinion, it is probably least important, (4) gas from the blood, and (5) the gas which is in the intestinal tract does not move forward due to some failure in the motility. In the normal adult, scout films of the abdomen usually reveal very little gas in the small bowel. Most of it is in the colon. This may be due to the greater ability of the small bowel to absorb gases or to pass them on into the colon. Some of the gas in the intestine is probably excreted from the blood. In children, however, this is not true, particularly in the infant. Here the small bowel often contains much gas. The gas which is ordinarily found in the flatus usually contains very little carbon dioxide or oxygen because these gases are easily and rapidly absorbed from the bowel and thrown out through the lungs. In herbiverous animals large amounts of gas are constantly being taken up by the food as it passes through the wall of the stomach and the cecum. Therefore, any condition which interferes with the return of venous blood from the intestine is likely to produce gaseous distention. Pneumonia, which interferes with the passage of gas from the lung, produces gaseous distention. This is also true of cardiac inadequacy or cardiac failure. Here, however, not only is gas not returned to the heart and thereby to the lungs for excretion, but due to the passive congestion there is diminished peristalsis so that gas is not carried forward. All other gases such as methane, carbon disulfide, in addition to carbon dioxide and oxygen, are absorbed, but nitrogen is poorly absorbed. Since four-fifths of ordinary air is nitrogen, the inhalation of pure oxygen may displace the nitrogen, thereby relieving intestinal distention.

Belching has been described and discussed previously in the chapter. Bloating has such a great and enormous variety of causes that many of them are intangible or

not discernible. Also, many patients complain of a false sense of flatus, and examination fails to reveal any abdominal distention. Constipation gives this feeling and yet it is not due to gas but rather to the mechanical distention of the rectum which gives the false sensation. However, constipation may act in the form of an obstruction so that gas may actually be trapped and there may be a great amount of gaseous distention. Therefore, flatus or flatulence, as it has been called, may be innocent or it may be extremely serious as it is seen postoperatively or in intestinal obstruction. For example, the causes may be as follows: the eating of certain foods which irritate the mucosa of the bowel and interfere with passage of gas through it or into the blood, food allergy and food overeating, anxiety or pain, cholecystitis, cold and upper respiratory infections, diarrhea in which the large bowel is constantly being emptied, and due to the contrary impulse, if there be such a thing, the small bowel is distended. The same picture is true of patient with the so-called irritable or sensitive colon. Along this same line, hemorrhoids or fissures or any other inflammation about the anus may produce an obstructive accumulation of gas. This may be due to a reflex spasm of the sphincter muscles, and in this way gas may be formed. Also the presence of a mild peritoneal infection should be considered; also, rarely, the cause of gas is due to intestinal parasites. The surgeon is particularly interested in the obstructive phases which may be the cause of flatulence. Before passing on to this consideration, it should be mentioned that vitamin deficiency has produced various gas patterns, some of which can be discerned by the expert roentgenologist who is familiar with this type of deficiency. This is particularly true of vitamin B deficiency.

Since most of the gas present in the gastrointestinal tract reaches the canal by air swallowing or by air suction, surgeons have resorted to the Levine tube or the Miller-Abbott tube to decrease pre and postoperative distention. In fact, many surgeons use the tube routinely following surgery.

Thus we see that the gastrointerocolic canal is a very complex system which makes life possible through its enzymes, which in turn are secreted because of nervous and hormonal influences; among the latter are "gastrin" to stimulate gastric secretion, prosecretin and secretin to stimulate pancreatic secretion, cholecystokinin to stimulate gall bladder evacuation, enterogastrone to inhibit gastric secretion, hydrocrinin to stimulate intestinal secretion, enterocrinin to stimulate the intestinal glands, duodenin to aid in carbohydrate metabolism and also to stimulate the islands of Langerhans. Also through these secretions digestion is maintained. The absorption of the digestive food products is made possible through their simplification and rapid absorption through the forces of selective absorption as well as osmosis dialysis. Last, we have seen that the bacteria in the large intestines are able to synthesize the vitamin K, and it has been thought by some that it may even help in the synthesis of thiamine, riboflavin, pyridoxine, pantothenic acids, and nicotinic acid.

STOMACH AND DUODENUM

Diseases of the Stomach and Duodenum

Diseases of the stomach and duodenum are either functional or organic. Perhaps functional disease paves the way for organic, especially in the case of peptic ulcer.

Congenital Anomalies of the Stomach and Duodenum

Congenital anomalies of the stomach and duodenum may be divided into (a) duplications, (b) diverticula, (3) atresias, (d) stenosis, (e) nonrotation and malrotation.

Duplications.—Duplications of the stomach and duodenum are rare. Several theories have been put forth as to the origin of these conditions. The most probable of the theories advanced has been that of Lewis and Thyng who found diverticula in various parts of the fetal alimentary tract of the pig, rabbit, cat, sheep, and man. They found that the outpocketings are most often seen in the ileum, and this corresponds to the greater frequency of duplications in this part of the alimentary canal. The duplications in these parts have been given many names in the past. They were formerly described as enterogenous cysts, enteric cysts, ileum duplex, giant diverticula, occlusion cysts, or duplications of the alimentary tract. It is perhaps best that we use the term duplications because this in reality is what they are. The duplications are found anywhere along the gastrointestinal tract, and since this discussion is limited to the stomach and duodenum, we shall discuss at this point only duplications of the two portions mentioned.

The abnormality which is present gives rise to the large sac filled with clear, colorless, mucoid substance which has been secreted by its own membrane. Very often this secretion is entrapped under a very high pressure and may induce necrosis and even sloughing of the lining membrane. At times the fluid becomes hemorrhagic. This may be due to local ulceration. If there is an opening into the bowel, duplication contents are similar to those of the intestinal canal. Sometimes the duplication has a separate blood supply; usually, however, the blood supply is the same as the organ which is duplicated. Therefore, it very often becomes necessary to remove both the duplication and the original normal structure. Duplications look very much like mesenteric cysts; however, the latter are lymphatic in origin. They have a thin wall and they can usually be shelled out from the adjacent viscera and from the mesentery, as a rule. The duplication has a thick, muscular wall and, as has been said, is usually very densely attached to the parent structure.

The symptoms and signs of duplication may vary; usually, however, they may be classed under three categories: (1) Those that resemble partial obstruction of the bowel; in addition, a mass can be felt; (2) those in which there may be pain due to the enormous amount of fluid present; (3) those which may press upon mesenteric blood vessels and produce necrosis, sloughing, and bleeding in the adjacent intestine. In the latter instance, of course, there is usually an opening which has been present or a new one which has been made, due to necrosis. Duplications of the stomach cause symptoms of epigastric fullness and discomfort. However, the majority of duplications cause colic and pain, vomiting, visible peristalsis, and all the other symptoms and signs of intestinal obstruction, partial or complete.

The diagnosis is made by a study of the symptoms and signs, and the fact that the condition is present in a child, a barium enema and barium meal give valuable information. Since the cystic structure in the intestines has a common wall at one point and usually the two cannot be

separated from one another without injuring the bowel and also since the arteries and veins of the contiguous portion of the alimentary tract usually course over the surface of the cyst, attempts to resect the cyst alone will be fraught with danger unless the blood vessels are interrupted; if they are, gangrene of the normal component occurs. Because of these conditions, operation usually consists of resection of the duplication as well as the parent organ. However, in the case of duplication of the stomach, Ladd elected to open the cyst and resect it and marsupialize the remaining portion. In some cases of duplication of the rectum and even duplication of the colon, it is possible to remove the cyst without removing the attached bowel. In practically every case that we have seen, the attachment was so close that the bowel wall was injured and had to be repaired.

Diverticula.—Diverticula may occur anywhere along the gastrointestinal tract as well as in the pharynx and esophagus. Diverticula also appear in the lower bowel, and the most common type is Meckel's diverticulum which will be discussed later. Diverticula of the stomach and duodenum also occur and may give rise to many symptoms. Diverticula of the stomach and duodenum may be classified as true or false. The true diverticula are those that contain all of the coats of the normal bowel. The false diverticula are those that occur as a result of inflammation or ulceration with the formation of a pouch which is made up of part of the coat of the bowel.

The symptoms and signs of diverticula in the stomach and duodenum are usually due to inflammation in the diverticulum. The changes within the diverticulum due to this inflammation may actually cause gangrene or perforation and peritonitis. If the diverticulum is inflamed without any of the results mentioned, the symptoms may be those of peptic ulcer in the stomach or duodenum. The diverticulum is diagnosed by careful x-ray examination with barium meal.

The treatment of the diverticulum consists of its removal. Several methods are available to the surgeon. Some authorities have recommended that the diverticulum be turned in. Since the penetrating vessels that surround it are tied, the sac will ultimately slough or cause its obliteration. It is better, however, to remove the diverticulum and close the opening. Cysts of the duodenum, as they have been called, are usually diverticula. The cysts may be enucleated or completely excised with the removal of the parent portion of the alimentary canal. The latter is difficult in the duodenum and would require, if near the ampulla of Vater, transplantation of the common bile duct. In most cases, however, it may be removed safely and the edges sutured. Should the bowel require resection, a posterior gastroenterostomy may be done or continuity established by anastomosis of the divided ends.

Atresias.—In our previous discussion concerning the embryology of the fore-gut, we have seen that the intestine goes through a so-called solid

phase. This is also true of the duodenum, and it is probably occasionally true of the stomach. The atresias of the intestine will be discussed later in the chapter. At this time we should point out that the atresias may be in the form of a diaphragm or a veil which completely blocks the lumen, or in the intestine it may end in an absolutely blind end with no continuity of the bowel except perhaps a very thin fibrous strand which may join the two ends together. The condition of atresia is distinguished from that of stenosis; the latter type implies a partial type of obstruction and will be discussed next.

The stomach is originally a straight tube which enlarges on its posterior side faster than on its anterior surface. As a result, this dorsal enlargement sags and becomes the greater curvature. The organ then rotates on its axis to the right; the right side becomes the posterior, and the left side becomes the anterior surface of the stomach. In the same way the anterior wall becomes the lesser curvature, and, as has been stated, the posterior surface becomes the greater curvature. This explains the innervation of the anterior surface by the left vagus and the posterior by the right vagus nerve.

Originally the stomach is laid down around the mesenteron, which is mucous membrane; then the mesenchymal elements surround this, and, last, the mesothelium covers it. It is easy to understand, therefore, that any one of the layers of the stomach may be involved in a congenital deformity. First, obstructions of the stomach in young children are usually encountered in the pylorus. This lesion is known as congenital hypertrophic pyloric stenosis. It is easily identified by its characteristic clinical symptoms and signs. Second, the pylorus may be narrowed without hypertrophy, a state which is infrequently encountered because it rarely gives sufficient symptoms in the child to warrant operation. Third, the stomach may be occluded by hands or adhesions in the outer layers. Last, the stomach is rarely obstructed by intrinsic or extrinsic tumors or cysts.

We have seen two cases of obstruction in the stomach due to a prepyloric membrane. Touroff and Sussman reported a case which resembles ours and which they state is the first to be reported in an infant. The literature reveals only two or three cases comparable to ours.

The history of our first case shows that the child apparently had no symptoms until three weeks before admission, and, therefore, the lesion was not related to a hypertrophic pyloric stenosis which usually is seen in about the sixth or eighth week of life. It is inconceivable that this diaphragm could have grown to its present size and thickness in three weeks; therefore, the lesion has probably been present since birth or shortly thereafter. Complete obstruction occurred while the child was in the hospital. The boy's vomitus contained no bile. There was little distention, and there were infrequent bowel movements of the starvation type; however, these contained bile. We concluded from this observation that the obstruction was above the ampulla and that the gastrointestinal tract

below the site of the occlusion was clear. *At operation, the diaphragm* was found to be approximately an eighth of an inch thick, and it was covered with mucous membrane on each side. The pylorus was patent and no other defects could be demonstrated. Accordingly, the diaphragm was divided down to its lumen which barely admitted the tip of a hemostat. The *incision* was made longitudinally and was closed transversely in the manner of Heineke-Mikulicz's pyloroplasty. The diagram illustrates the type of operative procedure. The child made an uneventful recovery and *his check-up films demonstrate that he has been entirely relieved* of his obstruction.

Atresias of the duodenum have been encountered more frequntly. Usually *the atresia is due to a persisting membrane or veil rather than a*

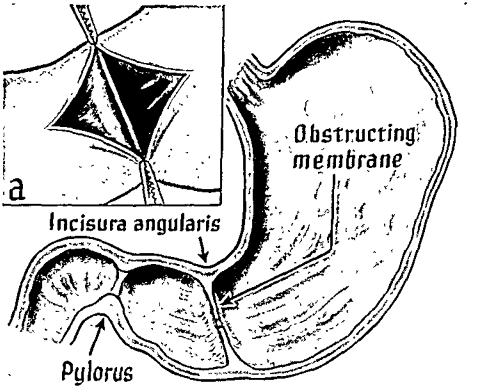

Fig. 272.—Diagram illustrating a very rare condition—prepyloric membranous obstruction. This was in a white boy 2 years of age who came to the hospital complaining of persistent vomiting. In the week prior to our examination he had had no bowel movements and enemata had been ineffectual. X-ray examination *showed* a greatly dilated stomach, due chiefly to gas but also to a large volume of fluid and food. Peristaltic waves were weak and ineffective. Two hours after the barium meal all of it was retained in the stomach and twelve hours after *ingestion there* was about 20 per cent retention. At operation the rare condition known as prepyloric membranous obstruction was encountered. Although this is not a complete obstruction, it was sufficient to produce *the symptoms and signs of a pyloric stenosis* from which it must be differentiated in the early weeks of life. However, at 2 years of age the diagnosis of *some* other anomaly must be entertained.

The cause of this obstruction is said to be due to the fact that in embryos thirty to sixty days vacuoles appear in the walls of the gastrointestinal tract, and *epithelial* septa completely block the lumen for a short period. Sometimes these septa persist and an obstruction results, but such membranes are rarely found in the stomach. There have been only two or three such cases reported so far as we are aware. *The* diagram illustrates the condition which was found and the manner in which it was corrected. *a.* Much of the membrane was removed through a longitudinal opening in the stomach and then the stomach was *closed in a transverse manner. The* child made an uneventful recovery. (After Berman and Ballinger: Quart. Bull. Indiana Univ. M. Center 4: 14, 1942.)

blind end which is seen in the lower ileum. The condition manifests itself by *the usual signs and symptoms of obstruction*; however, the vomitus is different than in the prepyloric or pyloric obstruction in that it contains bile. Distal to the obstruction is a small bowel which contains no gas and which has only within its lumen a few shreds of mucous cells which have been cast off. Proximal to the obstruction the bowel is greatly distended and sometimes reaches 3 to 4 cm. in diameter. Because of this great distention, necrosis and perforation may occur. The *meconium in intestinal atresia* has been of great value in suspecting the diagnosis, and this will be discussed later in dealing with obstruction lower down. However, it might be said here that in a normal child, meconium is composed of dead cells from the intestinal lining, various secretions from the stomach, intestines, liver, and pancreas, and material from the amniotic fluid which the baby is said to swallow in utero.

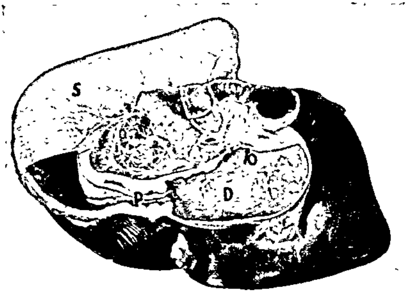

Fig. 273.—Congenital obstruction of the duodenum (second portion) due to atresia. *S*, stomach; *P*, pylorus; *D*, duodenum; *O*, obstruction. Forty-eight-hour-old infant. Death occurred before operation could be done.

Among the constituents of amniotic fluid is vernix caseosa and squamous epithelial cells, which are sloughed from the skin. The meconium of the normal baby, therefore, contains cornified epithelial cells which passed through the intestinal wall. In an atresia, of course, the intestine or colon will not allow them to pass beyond the obstructed point. Therefore, Barger has called attention to the fact that a specimen of meconium may be examined and a smear made on a glass slide. If this is washed with ether, then stained with Sterling's gentian violet, and then decolorized with acid alcohol, the decoloration removes the dye from all of the specimen except the cornified epithelil cells. In any newborn child with

intestinal obstruction, the absence of cornified epithelial cells in the meconium is a presumptive evidence of the atresia. However, the vomiting which contains bile, x-ray showing the pattern of distended bowel, and other clinical signs, such as distention above, will usually be sufficient to point to the correct diagnosis and, moreover, to the site of obstruction. Abdominal distention is present in a baby even though the obstruction is high. However, in duodenal obstruction this distention will be limited to the epigastrium, whereas in the obstruction lower down, the distention is very great, involving the whole abdomen. It has been our custom not to give barium by rectum if an obstruction low down is suspected. The barium enema will give valuable information in making the diagnosis and in excluding such anomalies as malrotation low down and diaphragmatic hernia. The presence of fluid within the abdominal cavity may be suspected from the x-ray films, particularly in babies, because of the separation of the bowel loops.

The treatment for atresia is prompt surgical intervention. The newborn stands operation well if a Levine tube is placed in the stomach and the baby's fluid balance is taken care of. The atresia usually requires resection, and this should be done under general anesthesia. The method of surgical treatment usually consists of division of the bowel and lateral anastomosis. If the bowel is obstructed by a membrane, this may be divided. However, in our experience, this has been extremely rare. If an atresia is single rather than multiple, the prognosis is fairly good. In the duodenum atresias are best treated by doing a duodenojejunostomy or an extremely high posterior gastrojejunostomy. The duodenojejunostomy is usually retrocolic as is also the gastrojejunostomy. Ileostomy is not tolerated by the newborn at all. If the ileostomy is done close to the ileocecal valve, there is a chance providing secondary operation is done within two or three days.

Stenosis.—The term stenosis is used to imply an incomplete obstruction, and this, too, may be due to a persistence of a vein such as we previously described. Stenosis of the bowel are not uncommon in the duodenum.

The symptoms and signs in early cases are, therefore, those of a partial obstruction, and there will be vomiting which will be persistent, some abdominal distention, loss of weight, and diminished number and size of stools. The vomitus is colored green because it is below the ampulla of Vater. However, occasionally the obstruction may be above the ampulla of Vater, and in these cases the stenosis resembles pyloric stenosis which will be discussed subsequently. In the older babies the symptoms and signs will be those of partial obstruction. The baby has difficulty in getting along with his diet. There is more or less persistent vomiting and failure to gain weight; dehydration takes place, and in most instances the baby has a progressively downhill course. However, some children may live on for long periods of time, not gaining and yet not losing,

simply because a small amount of food gets through the partial obstruction. In children, large peristaltic waves are easily detected, and in the duodenum the distention may be very great. X-ray examination, of course, aids greatly in making the diagnosis, although even here sometimes it is difficult, unless the obstruction is in the second portion of the duodenum, to distinguish between this lesion and that of pyloric obstruction.

The treatment is surgery, and the operation should be an anastomosis between the obstruction and an unobstructed portion of the bowel. In the case of the duodenum it will be a duodenojejunostomy unless it is very high. In such cases a posterior gastroenterostomy is indicated.

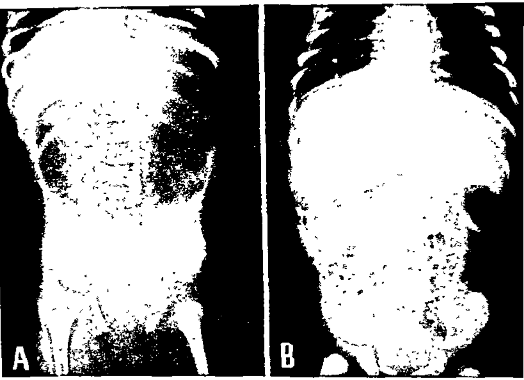

Fig. 274.—Congenital stenoses of duodenum. This was the case of a child, 6 weeks of age, who came to the hospital vomiting everything taken. *A*. X-ray photograph which clearly demonstrates the enormous dilation of the stomach and the first portion of the duodenum. This child was operated upon and the condition was found to be a stenosis of the duodenum at the junction of the first and second portion due to fibrosis of the wall of the duodenum The first portion of the duodenum and the jejunum were brought together with a side-to-side anastomosis anterior to the transverse colon. This child made an uneventful recovery. *B*. Postoperative films showing gas throughout the alimentary canal. (Case referred by Dr. William Browning.)

Nonrotation and Malrotation of the Intestine.—Although this subject belongs more properly to the midgut, we shall discuss it at this time since errors in rotation frequently produce obstructions to the duodenum, due to adventitious bands or adhesions.

Since the mid-gut shows the most complex developmental arrangement, congenital anomalies are most common in this region. The mid-

gut in its earliest development is a convex loop with its end attached to the duodenocolic isthmus and supported throughout its length by a common dorsal mesentery. In this mesentery runs the superior mesenteric artery. Until the end of the third week the mid-gut communicates with the yolk sac through the vitello-intestinal duct, but after this date the duct should normally close. Should it not do so or should its attachment persist, an anomaly commonly known as persistent vitello-intestinal duct and Meckel's diverticulum may occur. During the fifth week, as a result of the rapid growth of the midgut, it is extruded as a partly herniated loop through the umbilical orifice so that the liver may have room to enlarge. Between the fifth and tenth weeks, while the loop is herniated, rotation begins, and it is in this stage that variations may occur.

The intestine in this stage appears as a loop with a pointed dome, to which is attached the vitelline duct. There is also a lower projection which is to form the ileocecal juncture. This is seen as a sagittal protrusion. Rotation proceeds in a counterclockwise manner, and by the end of the tenth week a return of the extruded loop is begun back into the abdomen.

Since all the intestine cannot return at the same moment, it is supposed that the portion of the mid-gut which forms the duodenum and jejunum returns first and then the cecum and ileum follow. The last portion of the ileum to return carries the superior mesenteric artery with it, and its return is followed by the cecum and adjoining colon. Since this is true, it is apparent that the duodenum will cross behind the superior mesenteric vessels near their origin, whereas the colon will cross the same point anteriorly. Upon entering the abdomen, the ascending colon first lies upward and toward the left and has the ileum entering it from the right. Then it begins its rotation toward the right and downward so that it may come to lie in its normal position. After the tenth week there is some progress of rotation, and this continues to the time of birth and even later. Finally the mesentery becomes fused and is attached to the posterior abdominal wall.

In summary we may state that this process of development of the mid-gut to allow for its own rapid growth as well as the growth of the liver is fraught with danger and may be conveniently divided into three stages: the first stage, from the fifth to the tenth week, while the loop is herniated; the second stage, during the tenth and eleventh weeks, while the loop is rotating and going back into the abdomen; and the third stage, from the eleventh week until birth or even later, while the loop becomes fixed in its normal position and the mesenteries fuse. Dott has summarized the dangers of these stages as follows: During the first stage extroversion of the cloaca may occur. This implies that not only rotation is interfered with but that development of the mid-gut and hind-gut is imperfect. This anomaly is therefore incompatible with life and not of surgical importance.

During the second stage we find most of the errors which are encountered in surgery. These are listed by Dott as:

1. Nonrotations of the mid-gut loop in which the small intestine lies chiefly to the right of the midline and the cecum lies in the left ileac fossa or in the pelvis and is reversed so that the ileum enters it from the right. The ascending colon passes upward and to the left. The importance of this is that adhesions may adventitiously produce obstruction, and the small intestines and the proximal half of the colon remain suspended by a narrow pedicle (the duodenocolic isthmus).

2. Reversed rotation of the mid-gut loop. Instead of a counterclockwise rotation, as we have previously described, there may be a clockwise rotation through an extent of about 90 degrees. This would put the transverse colon behind the mesenteric artery and the duodenum in front. The intestine would otherwise be in a normal position except that its anterior and posterior surfaces would be reversed. The importance of this is the possible obstruction of the transverse colon.

3. Malrotation of the mid-gut loop. A variation of disorders may occur as a result of this error. For example, the small intestine may pass in front of the vessels to lie on the right side. This puts the cecum into a high position in the region of the pylorus so that the duodenum and ileum lie close together.

On the other hand, the small intestine may remain entirely on the right side of the artery where again the cecum and ascending colon are prevented from reaching the right ileac region and, of course, this would retain a long primitive mesentery. The practical importance of these arrangements is the liability to volvulus.

Based upon this study, Fraser has listed the congenital errors of the mid-gut as follows:

1. Congenital atresia
2. Congenital diverticula or fistula
3. Errors of rotation (congenital volvulus)
   a. Extroversion of cloaca
   b. (1) Nonrotation of midgut loop
      (2) Malrotation of mid-gut loop
   c. Local displacements

Causes of Errors.—Although no one can definitely state the causes of these errors, many explanations have been advanced. The following causes of errors in rotation have been suggested:

1. Errors occur at the site of embryological events such as obstruction where the anus (proctodeum) and hind-gut meet or where the mouth (stomodeum) and fore-gut meet or where the vitello-intestinal duct enters the mid-gut.

2. Vascular defects due to pressure on the arterial blood supply, such as duodenal obstruction from anomaly of mesenteric vessels.

3. Defective rotation as described by Dott. *Variations in size of the umbilical orifice may account for errors in rotation.*

4. Prentiss states that in embryos of *thirty to sixty days vacuoles* appear in the wall of the duodenum. *These epithelial septa completely* block the lumen. The remainder of *the small intestine remains open, although* vacuoles form in its epithelium. *Sometimes this impervious duodenum* of the embryo may persist as a *congenital anomaly. Simpson* speaks of this as the segmental *arrest of development during certain* known periods of embryological *sequence of events, such as tenth week* of fetal life, when the duodenum *and certain other portions of the intestinal* tract are practically solid *from proliferation of the lining epithelium* too rapidly for the increase in diameter of the gut.

5. Fetal disease (peritonitis) *or faulty development of the sympathetic* nervous system according to Davis and Poynter.

6. Hale has produced anomalies *in pigs experimentally* by withholding vitamin A in the mother's diet at certain periods of gestation.

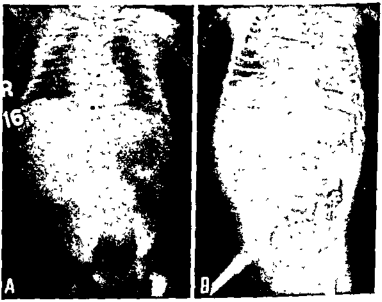

Fig. 275.—Malrotation. X-ray photographs of an infant, 5 days old, who had vomited since birth.

A. Scout film before surgery. The gas pattern is all on the left side; the stomach and duodenum are dilated. *B.* Lipiodol given by *mouth before operation.* Most of it is returned in the stomach. Note dilated duodenum. Only a small amount trickles through into loops of small bowel.

There had been an occasional passage of meconium. There was much distention and peristaltic waves could be easily detected going in various directions across the upper abdomen. Preoperative diagnosis was malrotation with obstruction of the duodenum due to *bands.* At *operation upon opening the abdomen* the ascending and transverse colon presented. There was great distention of the duodenum and stomach. *An obstruction was found in the second portion of* the duodenum due to direct pressure from the bands which connected the undescended mid-line cecum to the lateral wall of the abdominal cavity. The ileum entered the cecum from right to left. The duodenal obstruction was evidently due to the bands and also to the cecum which immediately overlay the third portion of the duodenum. The peritoneum was incised and the bands were divided, permitting the cecum to be transferred to the left side. After this was accomplished, the obstruction was released. The anatomical arrangement following operation was as follows: the duodenum descended in a straight line into the jejunum and was not covered by the posterior peritoneum. The ileum entered the cecum from right to left. The cecum was on the left side of the abdomen and the colon ascended on the left, and then by sharp curve it came down as the descending colon and sigmoid. After operation the child was entirely relieved of his symptoms. (Case referred by Dr. S. Kauffman.)

Method of Diagnosis.—The diagnosis of congenital anomalies of the small intestine is not always a simple matter. The clinical signs of obstruction may be variable and although vomiting, distention, absence of stools, and borborygmus are the cardinal signs, these may not be apparent early. For example, high obstruction is accompanied by early vomiting and little or no distention, and stools occur until the bowel below the obstruction is empty, whereas in low obstruction, vomiting is very late, and distention and absolute constipation early. Then, too, multiple lesions may be present. Careful roentgen ray examination by the barium enema, together with examination and manipulation of the abdomen under the fluoroscope, and shifting gas pockets, as described by us, aid greatly in locating the site of the lesion.

Farber emphasizes the value of studying the epithelial cells in the meconium. He states that the presence of such cells aids in the differential diagnosis by ruling out obstruction. Farber states that the absence of cornified cells in smears of meconium is proof of congenital atresia of the alimentary canal. Meckel's diverticulum without a patent omphalomesenteric duct may defy preoperative diagnosis.

Ladd has described two types of malrotation which are most commonly encountered. (1) Obstruction of descending duodenum with incomplete rotation of the cecum. One finds this organ just below the distal half of the stomach and bands of reflected peritoneum running from it or the ascending colon to the right posterolateral part of the abdominal wall. These bands run across the descending portion of the duodenum and obstruct it. Sometimes the cecum has proceeded farther, but as yet has incompletely rotated so that it lies directly over the duodenum. (2) Volvulus of the mid-gut. The mesentery of the small intestine lacks its normal fixation so that it has only a short rudimentary attachment just below the origin of the superior mesenteric artery.. When the intestine from the duodenojejunal juncture to the transverse colon is thus supported by an incompletely anchored mesentery, there may be a volvulus of the entire midgut. This rotation takes place in a clockwise *direction. Volvulus and an obstruction of the duodenum may be present* at the same time. Consequently it is well to speak of these two conditions together. With these lesions, of course, there will be great distention or dilation of the duodenum. If there is volvulus of the mid-gut, then the jejunum and ileum will be collapsed at first because duodenal contents cannot enter this obstructed segment. Later, however, there may be some gas in the obstructed portion of the bowel, due to local bacterial growth. The chief symptom of this condition is vomiting. The vomitus contains bile, but it is early and persistent. Distention is not very great because only the duodenum and stomach are dilated. It is, therefore, limited to the epigastrium. Dehydration takes place very rapidly, and fever which is probably due to dehydration occurs. In older children there is abdominal pain, nausea, vomiting, and symptoms and signs of partial obstruction. Hence, in these older children there is ab-

dominal distention, poor absorption of food, and intolerance to certain substances. The diagnosis of celiac disease may be erroneously made. However, the complaints which have been enumerated may be brought about by twisting of the mid-gut in a way that the terminal ileum is temporarily or partially obstructed. It is, therefore, important to examine by x-ray all the individuals who have so-called celiac disease. The scant film of the abdomen reveals the distended loop which usually helps in making the diagnosis. A barium meal should not be given as a rule. Barium enema may be used, and it will give a great deal of information, since the cecum is mobile and may be placed in an abnormal position. This is sufficient to make a diagnosis. In partial obstructions, barium by mouth may be administered if weak; however, this too may convert an incomplete into a complete obstruction.

The treatment for malrotations and nonrotations is surgical. There will be two types of lesions which will be encountered, according to Ladd. (1) When the ascending and transverse colon present and there is a duodenal obstruction. Here the obstruction of the duodenum results from direct pressure from the overlying cecum or by peritoneal bands which cross over the colon or cecum. This duodenal obstruction is relieved by an operation which was devised by Ladd several years ago. The operation is as follows: The posterior parietal peritoneum is incised just to the right of the cecum which permits clearing of the anterior surface of the duodenum. The cecum is transferred to the left side, and all pressure is thereby taken off the duodenum. No attempt is made to restore the normal anatomical position of the cecum. (2) A mid-gut volvulus; on opening the abdomen, the bluish-colored small intestine will present. The cecum and ascending colon cannot be found and often it appears as though loops of small bowel are herniating through the mesentery of another portion of the intestine. The only way to deal with this situation is to remove the whole mid-gut from the abdomen and place it on warm sponges; then the volvulus can be recognized. It has usually taken place in a clockwise direction and may go through an arc of 360 degrees. The volvulus is reduced by turning the mass in a counter-clockwise direction. As soon as this is done, the normal color returns to the intestine, but this may mislead the surgeon into believing that the operation has been completed. However, the cecum and ascending colon which now lie on the right upper quadrant must be free to transfer to the left just as in the previous instance. This can be rapidly done by incising the peritoneum to the right of the ascending colon. After this is slit, the duodenum will be seen coursing downward in the right paravertebral gutter joining the jejunum. The cecum and colon will lie to the left side of the abdomen. One last congenital anomaly should be mentioned; namely, that of a mobile cecum. Occasionally this produces symptoms because it lacks a normal posterior attachment. If there is a normal oblique attachment to the mesentery, then the mobile cecum can be tacked down posteriorly. If, in addition, the mesentery does not have

a normal posterior attachment, then it is technically easier, safer, and quicker to slit the peritoneum at the right of the hepatic flexure so that the entire right half of the colon shifts over into the left side of the abdomen. We have seen a congenital volvulus of the duodenal jejunal juncture which was treated by rotating the obstructed loop in a counter clockwise direction. We have also seen a malrotation or reverse rotation showing the superior mesenteric artery in front of the transverse colon and the duodenum in front of the arteries. We have also seen a very rare condition in which the transverse colon was behind the superior mesenteric artery, but so was the duodenum.

Congenital Hypertrophic Pyloric Stenosis

Characteristically this disease occurs in infants in the fourth to the sixth week of life. Although the cause of the condition is not known, it usually is in the male child, usually in the firstborn. There is no racial distribution, and heredity does play a role. The condition manifests itself as a pyloric tumor at birth, and although it cannot be felt at that time, the presence of such a tumor is generally agreed upon. It has been known to occur in premature infants and in stillbirths. We have operated upon one child who was born six weeks prematurely. The symptoms and signs of the lesion occurred when he was two weeks premature and we operated upon him successfully while he was at two weeks prematurity. Therefore, in reviewing the pathogenesis of the lesion, we may say that it is congenital. The other important pathogenic factors are work hypertrophy, pylorospasm, and a combination of pylorospasm and work hypertrophy. The pyloric tumor, together with edema of the mucous membrane from the mechanical irritation that has occurred, explains the clinical picture.

The onset of symptoms, usually in the second to fifth week of life, is that of vomiting without bile. This vomiting is not constant, although it is continual. The pathology is as follows: The pyloric sphincter becomes greatly hypertrophied and spindle shaped and fades off into the stomach side *but ends abruptly on the duodenal end.* Microscopically the important finding is the tremendous hypertrophy of the circular, smooth muscle layer, together with an actual increase in the smooth muscle fibers. Sections of the mucosal layer reveal edema and slight leucocytic infiltrations. The symptoms and signs are dehydration, vomiting, weight loss, scanty stools, alkalosis, if the vomiting continues, and peristaltic waves. The waves pass from left to right and are best seen immediately after feeding. Sometimes, while watching such a wave, it ends abruptly and the child vomits forcibly. One must be cautious in making a diagnosis on waves alone, since a normal infant may show small waves which pass across the abdomen. However, if the waves are large and if they can be easily seen, then there can be little doubt that this finding is pathognomonic. Palpation of a tumor is, of course, diagnostic. Usually it is best to attempt this palpation either immediately

after vomiting or after some sedative has been administered. The palpation of a tumor is said to be possible in over 98 per cent of the cases. This has not been our experience, although it can be palpated in a great number of cases, certainly much over half. The laboratory finings are not of much help. However, they may act as a guide in preparing the child for surgery if there is a hemoconcentration and if the serum protein is low. Therefore, it is our custom to do a regular blood count, and, in addition, a determination of the plasma protein and hematocrit by the copper sulfate method. This is now routine. X-ray examination is not of great help. If there is a pyloric obstruction, the baby may regurgitate and aspirate some of the barium. If there is not a pyloric obstruction, there may be sufficient spasm to mislead even the most experienced roentgenologist. However, the x-ray features of diagnostic value are gastric dilation, intermittent hyperperistalsis, greatly elongated pyloric canal, which is very small in diameter, delayed gastric emptying time. The differential diagnosis lies between pylorospasm, infectious vomiting, improper feeding, and intracranial injury; also achalasia of the esophagus. The condition has been described as persistent vomiting with no other signs of pyloric stenosis. It can be diagnosed by x-ray films which show the gastric cardia in a state of continuous relaxation with frequent regurgitation of the barium which has been given. Babies with this difficulty respond well to a therapeutic test of thickened feedings while they are kept in an upright position. Extrinsic obstructions such as malrotation volvulus and intrinsic intestinal obstructions or atresias must also be considered. Differential diagnosis in the latter group is difficult at times. Usually, however, in the extrinsic types of obstructions, the vomitus will be bile stained, since the obstruction is at a lower level. The same is usually true of malrotation, but a duodenal stenosis may be very confusing, particularly if it is above the ampulla, and sometimes this diagnosis cannot be made before operation. (See Figs. 280 and 289.)

The treatment for congenital hypertrophic pyloric stenosis is very satisfactory and consists of an operation which is designed to divide the hypertrophied sphincter muscle. (Fredet-Ramstedt pylorotomy.) The babies are usually prepared by subcutaneous saline and, if necessary, intravenous administration of blood or plasma, or both. It has been our experience that it is very easy to overhydrate these infants and, therefore, we are cautious to give only approximately 10 c.c. per pound of body weight. We also give vitamins C and K preoperatively. Usually we pass a small catheter down into the stomach, wash out the stomach, and leave the catheter in place until the conclusion of the operation, when it is removed. We have done all of our operations under local anesthesia, although it is possible to do them under general anesthesia, and some surgeons prefer this. We do not use barbiturates, or morphine, preoperatively; instead we prefer to give 1/500 grain of atropine sulfate and nothing more. We use 1/2 of 1 per cent procaine solution for local

infiltration without Adrenalin. We use a right paramedian incision, split the rectus muscle, and then divide the transversalis transversely. The pylorus is delivered, and a small longitudinal incision is made through the serosa. This is about one-half to three-fourths of an inch in length. The muscle is split with a hemostat, and the mucous membrane is allowed to bulge. The dangerous part of this procedure is the inadvertent injury or penetration of the duodenal mucous membrane. This can be avoided if care is taken on this side of the incision. Should this occur, the mucous membrane is sutured and the omentum is sewed down over the leak. Hemorrhage may occur if the transpyloric vessels are cut. These sometimes require ligation.

Functional Disorders of the Stomach and Duodenum

Functional disorders of the stomach are common. Indeed, the stomach has been called the "barometer of the body." Bad news, pain, worry, or excitement, may induce vomiting. Indiscretions in diet or alcohol may cause the same, or an inflammation (gastritis). However, by far the most common disorder (so-called "nervous indigestion") is intimately related to dysfunction of the autonomic nervous system, which produces spasm (pylorospasm, cardiospasm) or secretory disorders achlorhydria and hyperchlorhydria). The treatment, after ruling out organic disease, consists in dietary measures, sedatives, and antispasmodics, together with rest and freedom from adverse psychic disturbances.

Acute dilatation of the stomach is a very serious condition in which this organ becomes greatly distended with fluid and gas. Its walls are atonic, and the more they become distended with fluid, the more atonic they become. The patient regurgitates dark, foul fluid continually. This results in hypochloremia, alkalosis, dehydration, and often tetany. It is seen usually after operation but often following a severe injury, or even after extreme overeating. Sometimes it is seen in pneumonia. The cause of the loss of gastric tone is a reflex nervous mechanism. The treatment is by Levine tube and suction (Wangensteen). The prognosis may be serious.

Vomiting is brought about by contraction of the abdominal wall, descent of the diaphragm, reduction of gastric tone, and relaxation of the cardiac sphincter and the esophagus. The glottis is closed and respirations are inhibited. In intestinal obstruction, antiperistaltic waves originate in the small intestine. These force the vomitus through the stomach, which does not manifest such waves.

In 1813 Magendie removed the stomach of an experimental animal and substituted a bladder filled with fluid; injection of an emetic was followed by evacuation of its contents. If the abdominal muscles are paralyzed by curare, vomiting does not occur. In human beings the stomach plays a small but minor role in the act. The author demonstrated this in studying the mechanism of perforated peptic ulcer.

Vomiting is controlled by a center in the medulla, and the afferent fibers to this center may come from almost every region of the body. Stimulation of the fauces, the pharynx, the mucosa of the stomach, or other abdominal viscera, pain from the special sense (eyestrain, tinnitus, vertigo, etc.), and even emotional states, such as fear, sorrow, joy, and excitement, may result in vomiting. Last, the center itself may be stimulated by such drugs as apomorphine, producing emesis. There is also a reflex vagus stimulation probably by way of the carotid sinus, and the heart is slowed or even momentarily stopped. Even nausea causes a slowing of the pulse, and on this basis simple paroxysmal tachycardia has been treated with ipecac. It has been thought that this reflex slowing of the heart is a conservative mechanism, preventing the blood in the large abdominal veins from being forced into the right heart, causing right-sided failure, and if not, pulmonary edema.

Heartburn has been described previously. Many patients with ulcer have it, but not when the ulcer is active and they have hunger pain. The degree of stomach acidity is unimportant and heartburn occurs with achlorhydria. Alcohol, tobacco, eating too fast or too much, or certain foods may cause it. It is probably due to regurgitation into a sensitized esophagus and partly to reverse waves of peristalsis coming up from the stomach.

Smoking produces heartburn and nervous indigestion, and according to some it may play a role in the recurrence of peptic ulcer. It is said to inhibit or depress hunger motility, and often secretion as well. In some smokers, saliva is increased; in others, it is not. All evidence, experimental and clinical, does show that occasionally there is gastric retention and increase in acidity. It is perhaps the type of individual rather than the smoking, or the peculiar temperament which impels a man to smoke one cigarette after another that gives rise to nervous indigestion or ulcer.

Caffeine stimulates gastric secretion and acid and may cause "nervous indigestion" and may be related to the chronicity of peptic ulcer. In large doses it may produce ulcer in cats. Coffee in moderation shows no abnormal effects in man.

Alcohol is known to increase the secretion of gastric juice of high acidity. It may be a cause for so-called nervous indigestion, gastritis, and even peptic ulcer.

Injuries to the Stomach and Duodenum

Foreign Bodies.—Injuries to the stomach may occur from within by chemical agents (ingestion of acids or alkalis) or mechanical agents (glass, sharp instruments, pins, etc.) or from without by penetrating, perforating, or nonpenetrating wounds.

1. *Injuries from within* are caused by swallowing the irritating or obstructing material inadvertently or intentionally. The latter may be inadvertent in that the patient is not aware that the harmless substance

over a long period of time may be injurious. In this category belong the bezoars (phytobezoars, plant) and trichobezoar (hair balls) which may fill the entire stomach, causing serious symptoms. Lastly, parasites (ascaris and taenia), gallstones which erode through usually into the duodenum, and sequestra from bone may be called endogenous in origin. We have recently seen a mercury tip tube swallowed, and no doubt this is true of Levine and Miller-Abbott tubes, especially when they become knotted.

Chemical substances that are strong acids or alkalis will burn the mouth and esophagus before reaching the stomach and duodenum and will have "spent themselves" so that ordinarily they do not burn the

Fig. 276.—Corrosive gastritis. The x-ray photograph is that of a child (D. P.) 18 months old who drank some "plumber's soldering fluid" or flux made from hydrochloric acid, zinc scraps, and tallow. This child presented few symptoms except restlessness and anorexia for about ten days; then vomiting occurred and it became progressively worse Finally, there was a complete obstruction which is readily seen in the x-ray photograph. It will be noted that the lower two-thirds of the stomach are occluded except for a very fine line (arrow). This child was treated ultimately by a high anterior gastroenterostomy. At the time of operation the interior of the stomach was inspected and found to be a mass of soft, bleeding granulation tissue The gastrojejunostomy was done above the area of obstruction and the child made a smooth recovery. Recent follow-up shows the child to be in normal condition. (Case referred by Dr M. Winter.)

gastric mucosa. Weaker acids and corrosives burn the stomach and duodenum. In the latter group are zinc compounds, ammonia compounds, acetic acid, etc. We have seen a case of corrosive gastritis that illustrates the problem. A child 18 months old drank some plumber's "soldering fluid" or flux made from hydrochloric acid, zinc scraps, and tallow. The child presented few symptoms except restlessness and

anorexia for about ten days. Then vomiting occurred which became progressively worse. Finally there was complete obstruction which was demonstrated by x-ray as involving the lower two-thirds of the stomach. A high anterior gastroenterostomy was done and the child made a smooth recovery.

Mechanical objects usually pass through the pylorus even if sharp. However, the large ones (bezoars) will be retained. Gallstones will pass down to the ileocecal valve or even to the rectum where lodgment may occur. Sharp instruments or needles may leave the stomach and wander into other viscera or the abdominal wall.

The diagnosis is made by the history, which may be misleading in that the foreign body was aspirated and not swallowed, or in the case of children or dements it may have been lost or inserted into the rectum or vagina. The x-ray examination with barium for radiolucent objects and without barium for others is indispensable.

Treatment is usually nonsurgical. Practically all small foreign bodies will pass through the pylorus, including open safety pins, needles, and straight pins. For the latter group we have given mashed potatoes mixed with long fiber cotton, assuming that this would envelop the sharp end. On a few occasions we have had to remove the open safety pin or a large foreign body (phyto- and trichobezoars) through a gastrotomy. The incision is made longitudinally and closed transversely.

2. *Injuries from without* are not always easy to diagnose. Penetrating and perforating wounds may be traced fairly accurately and the injury may be suspected. However, in perforations without external wounds the diagnosis may be more difficult. Traumatic retroperitoneal rupture of the duodenum has been reported, and we have seen two cases. We have encountered four cases of ruptured stomach without external wound: one in which a chronic peptic ulcer was present and the blow on the abdomen in an auto accident caused the perforation; two were due to fractured ribs which had penetrated the abdomen and stomach; and one without apparent cause except the external trauma. Most of our cases presented the perforation in the jejunum just beyond the ligament of Treitz and on the mesenteric border.

Diagnosis is made from the history and symptoms which consist of a rigid abdomen, absence of bowel sounds, pain in the left shoulder usually, and vomiting and constipation. X-ray examination in the upright and lateral decubitus positions shows free air in the majority of cases.

Treatment consists of immediate operation after the patient has been treated for shock. In all stomach injuries the lesser peritoneal cavity should be opened through the gastrocolic omentum so that the posterior wall of the stomach as well as the pancreas, may be inspected. Postoperative care includes Levine tube with suction chemotherapy, attention to water balance, and blood volume replacement.

Inflammation of the Stomach and Duodenum

Inflammations of the stomach and doudenum may be due to chemical, thermal, mechanical, and bacterial causes and to the little understood factors which cause it to become ulcerated. In addition, gastric inflammations are associated with *Bacillus coli* systemic disease such as pernicious anemia, tuberculosis, and syphilis as well as local neoplastic disease.

The stomach and first part of the duodeneum in healthy adults are usually sterile except after a meal, yet inflammations due to bacterial causes occur. Nonspecific types are acute, and chronic *acute gastritis*, which may be mild and are caused by any of the agents previously mentioned as well as by bacteria after the ingestion of grossly contaminated food. A form known as phlegmonous gastritis (acute suppurative cellulitis of the stomach; gastric erysipelas) is a rare highly fatal disease. It is caused by alcoholic injury to the wall of the stomach and subsequent infection by streptococci, *Bacillus coli*, and other organisms. It is perhaps comparable to gangrenous stomatitis and is the soil rather than the seed. It may be produced in dogs not by bacteria alone or bacteria and ground glass but by alcohol, then streptococci.

The process begins in the mucosa and quickly spreads throughout the thickness of the gastric wall. Occasionally the duodenum is involved. Suppurative peritonitis ensues in over one-third of the cases. The symptoms are persistent vomiting, severe pain, abdominal tenderness, and rigidity. Diagnosis is difficult, and in an alcoholic, perforated ulcer is often thought of. The true nature of the disease is discovered at operation. The prognosis is very grave and surgery offers little. Chemotherapy and antibiotics should be given. Rarely a case survives after gastrectomy.

Chronic gastritis is a vague entity which has been regarded as a complication of organic disease (ulcer, carcinoma) by some and as a forerunner of these diseases by others. The superficial types, as seen through the gastroscope, show some hyperemia; the atrophic variety is seen in pernicious anemia and corresponds to the smooth pale tongue and the pale atrophied vaginal and rectal mucous membrane often seen in the disease. Hypertrophic and postoperative varieties have also been described. Diagnosis can be made by fluoroscopy and gastroscopy; however, an organic lesion must be ruled out in every case.

Syphilitic gastritis occurs in the secondary and tertiary stages of the disease. In the latter, gross deformities occur as a result of infiltration of the submucosa. The diagnosis should be suspected when a young individual with stomach complaints is found to have a funnel deformity of the stomach resembling that of diffuse scirrhous carcinoma but much more pliable when examined with a barium meal and fluoroscopy. In addition, the stigmas of syphilis are present. At operation, resection is done and the true morbid anatomy discovered by microscopic examination of the excised tissue.

Tuberculosis of the stomach is uncommon and occurs as an ulcer in the pyloric region and fundus. Infection is probably hematogenous or lymphogennous rather than mucosal. Vomiting, emanation, and diarrhea are the most frequent symptoms. The diagnosis is difficult especially in children and cannot be made with certainty by any method. In adults surgery is indicated and biopsy should be done.

Duodenitis is frequently reported in x-ray studies. It probably follows somewhat the same pattern as gastritis.

Peptic Ulcer

The exact cause of the ulcers which form on the lesser curvature of the stomach or in the first portion of the duodenum is unknown, and various theories have been advanced to explain them. In fact, the term gastroduodenal ulcer is probably a misnomer, since ulcers of the stomach are in many ways different from those of the duodenum. The latter gives a slightly different clinical picture (discomfort appears later after the meal) and a greater tendency to perforation, and, if hemorrhage occurs, the position of the ulcer is posterior. The former has a greater tendency to bleed and obstruct, but, most important, the possibility of carcinoma is from 10 to 14 per cent, although this figure includes those gastric ulcers which were ulcerating carcinomas from the start. The positions are so variable that one is not justified in speaking of a single area as being ulcer bearing, although the magenstrasse of the lesser curvature is the most common site. Ulcers may be high up on the posterior wall, in the cardia, but rarely along the greater curvature (where carcinoma is more common) and in the duodenum down to the ampulla. Ulcer of the duodenum is far more common and is present in acute or chronic form in 5 to 10 per cent of the adult male population. They may be single or multiple. Among the causes which have been postulated are mechanical causes (trauma, vascular lesions, spasm of the pylorus). Some mechanical factors (trauma) are mentioned under miscellaneous causes. Often many causes are at work simultaneously. Secretory causes (an alteration in the gastric juice or in the normal resistance to it in the mucous membrane). Ulcers are usually encountered with high gastric acidity. Is this cause or effect? Acid is an inhibitory agent and stimulates the formation of mucin. The mere occurrence of a high acidity does not mean that a peptic ulcer will develop any more than the presence of streptococci in the throat means a streptococcic pharyngitis. In the latter case, the local immunity of the individual, if unimpaired, prevents this from occurring. In the former case, the protective mucin and neutralizing pancreatic juice also protect the tissue. The occurrence of an ulcer may be attributed to some breakdown of the protective mechanism. Mucin is protective in that it presents a slippery surface to irritants, it combines with and neutralizes the acid; when acid is secreted in large amounts, the mucus precipitates and forms an insoluble tough coat. In the duodenal cap there is less mucus, and it is

brushed aside by the chyme, leaving the mucosa unprotected. This was the basis for the author's experiments with duodenogastric intussception. These findings explain the fact that ulcers may occur with low acidity or achlorhydria and may not occur with high acidity or, having formed, may heal in the presence of hyperchlorhydria. It is surprising how little acid is required to produce a peptic ulcer in the absence of mucosal protection. This is exemplified in peptic ulcer in Meckel's diverticulum.

The first part of the duodenum is an acid area with an average pH of 5.6 in the fasting state and of 5 after an Ewald meal, but free acid is usually not present; and neurogenic causes (a constitutional susceptibility to the disease in certain individuals) in which ulcers occur run a natural course irrespective of treatment. However, complications may require treatment. The increase of ulcer in civilian population during the London blitz and in soldiers after the fall of Dunkirk illustrate the role of neurogenic causes. Gastric ulcers increased in members more than duodenal.

Miscellaneous Factors.—Infections in the sinuses, teeth, tonsils, appendix, prostate, and cervix uteri formerly regarded as silent and symptomless foci apparently play no role in the causation of ulcer (see Chapter 4).

Acute peptic ulcer may follow various injuries, namely, burns, Curling's ulcer, intracranial and spinal, fractures of long bones, and abdominal wall. It is also seen after operations such as thyroidectomy for thyrotoxicosis, intracranial operations, resection of the colon for carcinoma, cholecystectomy, pneumonectomy, drainage of lung abscess, spinal fusion. Last, it is sometimes seen in diabetic coma.

Dietary effects have been mentioned under the physiology earlier in this chapter. It is very doubtful if any dietary indiscretion not excluding alcohol is per se the cause of an acute or chronic ulcer. Perhaps the constant consumption of alcohol may play a role in susceptible individuals.

Experimental Studies.—

The injection of histamine in beeswax permits gradual liberation of histamine and the production of a sustained hyperchlorhydria with the formation of ulcer. Histamine inhibits the production of mucus and pepsin. Vagotomy inhibits the production of acid and also mucus. Vagotomy does not protect the experimental animal from histamine-induced ulcers.

Virtually all organs and tissues sewn experimentally into the gastric wall, including the stomach itself, except gastric epithelium, ultimately undergo digestion and fibrosis. Any tissue implanted which becomes covered by gastric epithelium is safe from further digestion. Jejunal transplants sutured into the stomach tend to inhibit ulcer, but when histamine in beeswax is injected, ulcer develops. Some authors have reported that there is an inhibition of gastric secretion following the sulface implantation of a portion of the jejunum as a pedicle graft. Other experimenters have not been able to verify these findings. Also, in the Mann Williamson dogs, ulcer develops after jejunal transplants. Most of the recent articles concerning the causation of ulcer have placed a major emphasis on gastric acidity. But ulcer does not develop in all cases of hyperacidity, and it may heal in the presence of hyperacidity, both in experimental animals and in man. Frequently pylorospasm has been invoked as a possible

cause of ulcer, and this in turn has been said to be due to an increase in hydrochloric acid. All experimental evidence to date shows that hydrochloric acid in the duodenum of the normal dog with concentration equal to or exceeding that of the stomach does not produce pylorospasm. In fact, the predominant effect is inhibition of the entire region of the sphincter.

Trauma is certainly not essential to the formation of ulcer. An isolated segment of the duodenum, jejunum, ileum, or the colon of the dog may be successfully implanted into a defect in the stomach; if the transplant has its blood supply, it will remain grossly intact and of normal appearance for about a year. In a somewhat similar manner the spleen, the kidney, and the pancreas of a dog may be mobilized and sutured into a defect in the gastric wall. If this is done with care not to injure the blood supply of the transplant, it will remain undigested for many weeks. The fibrous capsule of the sutured organ may be first removed so that the gastric juice has direct access to the parenchyma causing the tissue to be partly digested away, but in time an epithelial covering of gastric mucous membrane will grow out and finally cover the transplant.

Pure gastric juice has the capacity to destroy and digest all living tissues, including the wall of the stomach itself. Pure fundus secretion can be obtained by constructing in the dog the Heidenhain or Pavlow accessory stomach pouch or one of the more recent modifications. When tissues are implanted into the stomach wall of the isolated Pavlow or Heidenhain accessory stomach or in the total isolated stomach, the transplant promptly becomes excavated by the digestive action of the gastric juice. Death from hemorrhage takes place within a few days.

The exclusion of bile in the upper intestinal tract may be followed by duodenal ulcer in the experimental animal. This has also been proved in man. On the other hand, certain kinds of external biliary fistula may divert the bile from the duodenum for many months without causing ulceration. Exclusion of the pancreatic juice similarly may be followed by ulcers, but not invariably so. Recently, with the development of the operation of pancreatectomy, according to the Whipple technique, very few ulcers have been reported, although it must be said that at the time that this operation is done, partial gastrectomy is done also. If the duodenal juice is excluded from the intestine by operation which removes the duodenum and also prevents bile and pancreatic juices from entering the bowel, ulcer does not develop. It is perhaps correct to assume that the absence of pancreatic juice, bile, and duodenal juice or possibly any one of these juices from the upper intestine may cause an ulcer of the duodenum. The protection afforded by these secretions is said to be due to the neutralization of the hydrochloric acid. The effective substance is probably sodium bicarbonate; since it is in greater concentration in the pancreatic juice, it makes this secretion most important.

It is probably not so much an increase in the acidity but rather an increase in the amount of secretion or rather a hypersecretion of the normal juice with deficient neutralization that plays a role in the causation of ulcer. On the basis of this information it is assumed that the patient with ulcer secretes more gastric juice in response to food than does the normal person; also, and what is more important, he secretes more gastric juice when there is no obvious stimulant.

Recent studies have shown that patients with ulcer do not secrete any more gastric juice at night than do normal patients. However, if hydrochloric acid is the chief factor in ulcer distress, and delayed healing, it is essential that more attention be focused on the nocturnal phase of gastric secretion, regardless of how the patient feels during the night and regardless of the volume of gastric juice and the concentration of hydrochloric acid. While ulcer patients may not secrete more gastric juice or hydrochloric acid than the normal person, ulcer patients retain more of the juice and acid in their stomachs at any one time. During the night, therefore, the hydrochloric acid of the stomach may undo in part what neutralization accomplishes during the day, and during the night there is no food in the stomach, or liquids. The latter have a diluting effect.

The meal solids perform the neutralizing effect because of their acid absorbing power. Feedings during the night are therefore essential or night secretion should be reduced. While the foregoing findings were true in extensive tests, many observers have not verified these findings, stating that there is no increase in the amount of secretion during the night.

Chronic peptic ulcer does not occur in patients with complete and persistent achlorhydria. It would seem that the paramount importance of acid seems inescapable. Pepsin greatly facilitates this process, but it alone will not destroy the mucosa. Although evidence is lacking for the findings of chronic ulcer in the presence of achlorhydria, yet various cases have been reported in which at least transient achlorhydria was present. Furthermore, many cases are known to occur where the acid content is extremely low.

An attempt to produce ulcer experimentally by ligation of gastric vessels was unsuccessful in most animals; however, in rats this may be accomplished. Infarcts do occur which do form ulcers, but these usually heal spontaneously.

Acute ulcers have been observed in experimental burns. The ulcers are thought to occur as a result of mucosal congestion with associated increase in the susceptibility of the mucosa to slight trauma in the first stage in the pathogenesis of experimental ulcers. Burns may be complicated by shock and infection; it is the shock rather than the infection which is presumably the cause of the mucosal congestion. The detailed pathological evidence demonstrates that the final stage of duodenal or gastric ulceration in these dogs is a corrosive and not a local infectious process.

The over-all picture as to the probable cause of gastric ulcer has been summarized in four words: hypermotility, hypertonicity, hyperperistalsis, hypersecretion. It should be emphasized that many observers regard gastric and duodenal ulcer as distinct entities. This is certainly true as regards their respective potentialities with regard to cancer which is common on the gastric side and almost nonexistent on the duodenal side.

The incidence of ulcer was definitely increased during the London blitz and after the fall of Dunkirk. Peptic ulcer has been said to be a constitutional disease, running a natural course, irrespective of treatment. Complications, of course, require active treatment. It has also been called a psychosomatic disease, and the evidence for this is good.

Recent studies of duodenal ulcer have been made to correlate the psychosomatic changes with the activity of the ulcer. A distinctive pattern is said to be present not only in the duodenum, but in the digestive tract as a whole and also in the constitutional behavior of the patient. This pattern is said to be characterized by hypersensitivity, hyperirritability, hyperactivity, which involves the affected duodenum, the digestive tract as a whole, and the personality.

It has been previously observed that patients with an ulcer have a decrease in gastric mucus, and we have demonstrated to our satisfaction that it is the mucin which has the greatest protective value against the erosion by gastric juice in the experimental animal. However, in a recent series of tests, the mucin content in human peptic ulcer and gastritis was within normal limits. This was shown to be true in human beings as well as in experimental animals. This is contrary to the previous conception that a lowered mucin content exists in peptic ulcer and is of importance in its pathogenesis. No other clear evidence can be found of any difference between the mucin content in the gastric juice of healthy individuals and that of individuals suffering from various gastric disorders. It is well to say in this connection that the gastric acids in this particular group of patients was within normal limits. There was no reason for the mucin to be greatly increased; that is, because there was no calling forth of the mucin by an increase in the hydrochloric acid. In this study the average mucin content of the gastric juice varied from 0.15 to 1.5 per cent, the average being about 0.5 per cent.

Recently the effects of vagotomy have been studied by many surgeons after the pioneer work of reviving this operation by Dragstedt and co-workers. The exact cause

for the striking relief which patients derive from vagotomy is not entirely known. There may be several explanations: (1) the effect of the anesthesia that has been used in the patient during the operation, (2) the interruption of sensory pathways, although the sense of pain can be interpreted, as proved by the introduction of hydrochloric acid, which the patient feels, (3) the absence of free hydrochloric acid, (4) the decrease or absence of the peristaltic activity of the stomach.

Peptic ulcer may occur beyond the first portion of the duodenum; although this is unusual, it occurs regularly enough so that the surgeon must be on his guard unless he misses one of these ulcers. The most frequent site is the medial aspect of the superior duodenal angle, slightly within the initial portion of the descending duodenum, this being the area beyond the bulbar vertex, including the supra-ampullary region. The lesions are less frequently found as one approaches the ampulla, and they are exceedingly rare beyond this area.

Intensive experimentation has been done in an effort to evaluate the various types of operations for ulcer. *Gastrojejunostomy* is said not to offer much protection against the formation of ulcer induced by the injection of histamine in beeswax to expedite its occurrence. Our experiments show that it is one of the very best ways to prevent ulcer induced by histamine in beeswax. *Gastric resection* or antral excision in which the gastrojejunostomy of the Billroth II type is done does not protect animals against development of ulcers. The operation fails to reduce gastric acidity adequately and must be considered unsatisfactory. *Extensive gastric resection*, which controls the gastric acidity, ensures against recurrent ulcers, and leaves a residual pouch large enough to provide adequate gastric capacity, would appear to be the most satisfactory operation. Following the anastomosis of the first portion of the jejunum and an inversion of the lesser curvature according to the Hoffmeister pattern, the experimental animal is completely protected against ulcer. This is especially true if a short afferent loop has been used. The Finsterer *antral exclusion* without excision of the antral mucous membrane is followed by erosions of the gastric pouch. If the mucosa is excised and a three-fourths resection is done, animals do not get ulcer. Antral resection plus total intragastric regurgitation is found to enhance the possibility of jejunal ulcer rather than to protect against ulcer. *Fundusectomy*, with *gastrojejunostomy*, appears to furnish satisfactory protection against the development of jejunal ulcer, although this procedure offers less protection than gastrectomy as previously described. *Hemigastrectomy* does not furnish adequate protection. *Devine exclusion* with total intragastric regurgitation is unsatisfactory. *Resection* or *segmental* resection is not *conclusive*. The clinical limitations of such an operation are obvious. Vagotomy does not protect the animal against ulcer produced by histamine.

Summary.—Extensive three-fourths resection, including the antrum or at least the antral mucosa, and anastomosis with a short proximal afferent loop and small stoma is the operation of choice from the experimental angle, although if histamine in beeswax is used, posterior gastroenterostomy is equally efficacious in dogs as shown by us (J. F. Boyd and the author).

In a review of the bacteriology of peptic ulcer which was carried out to determine whether or not infection played a part in the causation of peptic ulcer, it was found that in most cases bacteria was isolated in carcinoma in nine out of ten cases, whereas in only sixteen in forty cases could any bacteria be isolated in benign ulcers.

Experimentally the use of omentum to close perforations of the stomach where no other tissue is available has been found to be satisfactory.

Recent studies on the bacterial flora in the abdomen following perforations of peptic ulcers show that practically all perforated ulcers have bacterial contamination in the peritoneal cavity soon after the perforation of the ulcer. Gastric acidity is low at the time of perforation, if not shortly before, and bacteria are to be found in gastric contents. The role of the chemical peritonitis is to favor the bacterial peritonitis which causes death. The time element, of course, plays a role, but this is thought to be

due to the extensiveness of the infection rather than to the secondary invasion by bacteria. Gastric juice poured into the peritoneal cavity is not lethal. It is true, however, that the mixtures of bile and pancreatic juice are occasionally lethal.

After a rather complete review of the literature on methods of closure of the duodenal stump in gastrectomy or pylorectomy, we are convinced that it is not the method of closure which leads to leaks but rather an interference with blood supply. Recent extensive dissections on the cadaver have shown that the blood supply of the duodenum is a very important factor in leakage after gastrectomy from the duodenal stump, adequate circulation must be preserved. The arteries of the duodenum are really end arteries, and there is a lack of intramural or marginal anastomosis. This finding is important to demonstrate the fact that due to the poor anastomosis of the duodenal vessels, inversion of the duodenum to the point of pancreatic attachment so that collateral circulation may provide nourishment is necessary.

Summary of Etiological Factors.—After carefully reviewing the enormous volume of clinical and experimental studies of peptic ulcer, one is struck by the fact that here is a disease which is, in most instances, the result of a failure of compensatory mechanisms properly to protect the wall of the stomach or of these mechanisms having been tried to the "breaking point" by gross indiscretion. In other words, "it takes two to make a bargain"—the "insult" and the failure of nature adequately to protect or repair the injury after it has occurred. There is no doubt that the "antigen" is mediated through excessive acid and the "antibody" or protection is the mucin which is at least part of the protective mechanism employed by nature in all of the mucous membranes of the body. Behind this unbalance lies the abstruse effect of a constitutional factor difficult to define and vaguely described as psychosomatic in origin. It is perhaps true that it is not the drink but the drinker, not the tobacco but the smoker. These problems may be solved some day by early training in environmental adjustments, although peptic ulcer is not too rare in children between the ages of 2 and 7 years. A prophylactic training of the central nervous system, so that it may take the ordinary adversities of life with the same equanimity as the autonomic nervous system takes the task of making its adjustments through compensatory mechanisms, may be a means of decreasing peptic ulcer as well as other psychosomatic diseases.

Pathology.—Peptic ulcers may be acute with much inflammatory reaction. These are usually but not invariably superficial and have little fibrous tissue around them (erosions of Dieulafoy) in contradistinction to the chronic fibrous (callus) ulcer which corresponds to ulcers elsewhere (see Chapter 6) which have developed granulation tissue but have not been covered with epithelium as in varicose ulcer. The granulation tissue changes to scar tissue, leaving a pale, hard, cicatrized bed over which epithelium will not grow. In addition, there is venous and lymph stasis with local anoxemia. Add to this its firmness, and it becomes evident that the edges cannot collapse or fold over and heal. This chronic ulcer is more apt to be on the posterior side. Also, like ulcers elsewhere, this fibrous bed may break down and ulcerate more, leading to erosion

into a blood vessel or adjacent organ as the pancreas. Ulcers may occur anywhere in the stomach, but over 60 per cent occur on the lesser curvature within 6 cm. of the pylorus. On the duodenal side there is greater

A.

B.

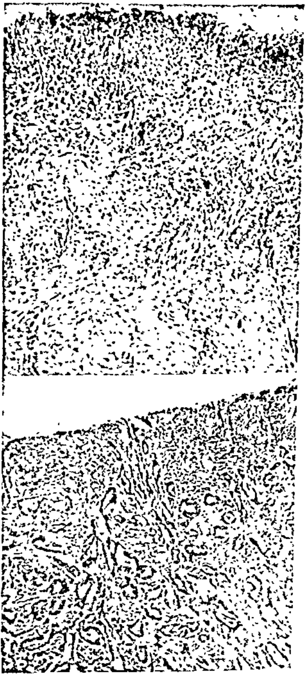

Fig. 277.—*A.* Low-power photomicrograph of a gastric ulcer. Due to the high acidity, the mucosa has been digested away. *B.* Malignant gastric ulcer. No free acid is present and therefore there has been no mucosal digestion; only slight erosion of the mucosa due to the growth. Note extension of the carcinoma into the submucosa.

variability, but the most common site is within 1 cm. of the pyloric ring (40 per cent) without about equal distribution between the anterior and posterior walls. In about 7 to 10 per cent there are both gastric and

duodenal ulcers. Necropsy statistics show gastric and duodenal ulcers to occur in about the same ratio; however, clinically duodenal ulcers are seen 10 to 1.

Complications of ulcer are hemorrhage, perforation, obstruction, and, on the stomach side, carcinoma. *Hemorrhage* occurs in both gastric and duodenal ulcer in some degree in over 30 per cent. It is said that hemorrhage is a more common complication of gastric than duodenal ulcer. Our experience does not bear this out, particularly in gross hemorrhage, which is more often duodenal due to a posterior ulcer eroding into the gastroduodenal or superior pancreatic duodenal arteries.

Hematemesis (vomiting of blood) may occur from various causes. A common error is to regard the bleeding from ruptured esophageal varices (due to cirrhosis of the liver) as a bleeding peptic ulcer. The former occurs without previous gastric symptoms; the latter may also occur without gastric symptoms, but this is rare. Parenthetically another common mistake is to interpret the gastric crises of tabes as evidence of organic disease of the stomach. In tabes there is severe pain but no vomiting. Diseases which may cause gastric hemorrhage are (1) trauma to the stomach by mechanical or chemical agents, (2) peptic ulcer, (3) benign or malignant neoplasms, (4) ulcerations associated with nephritis and severe toxemias, which may also produce gastritis with hemorrhage, (5) hepatic diseases (Laennec's cirrhosis, biliary cirrhosis, Banti's disease, hemolytic jaundice, anemia, phlebitis of the spleen or pylephlebitis, severe jaundice), (6) infectious diseases (yellow fever, pneumococcic infections, septicemias, scarlet fever), (7) blood dyscrasias (pernicious anemia, leucemia, purpura, hemophilia) or altered blood chemistry (phosphorus and arsenic poisoning, uremia, severe icterus, and cholemia), (8) heart disease with passive congestion, (9) tabes with gastric ulceration, (10) miscellaneous causes, some of which are vague and probably inaccurately diagnosed, such as vicarious menstruation and nervous disorders, (11) hereditary hemorrhagic telangiectasia. Gastric hemorrhage in the newborn is seen in severe icterus, infections, and toxemia; however, peptic ulcer in the newborn has been reported.

Perforation of the *acute* variety occurs in about 5 per cent of the ulcers of the stomach and duodenum. Slow or chronic perforations and subacute (forme fruste) types occur in 25 to 28 per cent of the chronic ulcers. Chronic perforations may have a thick fibrous wall and resemble a diverticulum on the x-ray. Perforations into the pancreas are not uncommon and may evoke considerable reaction in the pancreas, producing in some cases a low-grade parenchymatous pancreatitis. Acute perforations are said to occur more frequently on the gastric side; however, we have found the duodenum the more common site; perhaps this is due to greater number of duodenal ulcers encountered. Acute perforations are usually anterior and therefore they cause a chemical peritonitis which is soon converted into a bacterial infection because acids are low at the

time of perforation and food is contaminated. The amount of food which enters the peritoneal cavity and the length of time it is permitted to remain determine the extent of the bacterial invasion.

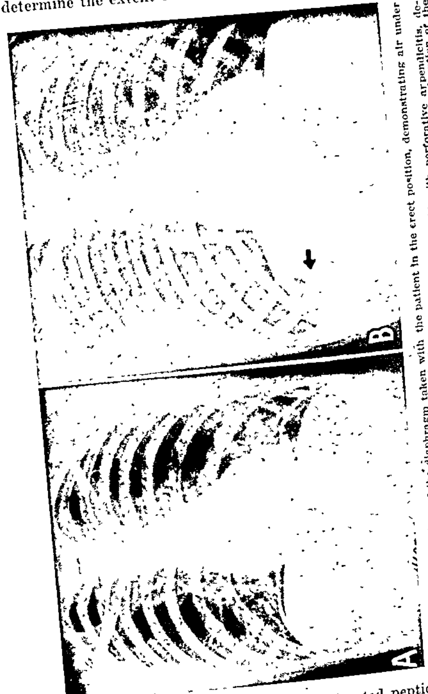

Fig. 278.—*A*, Flat plate of the diaphragm taken with the patient in the erect position, demonstrating air under the diaphragm, the result of a perforated peptic ulcer. *B*, Subphrenic abscess with air in the abscess cavity. The patient, a child with perforative appendicitis, developed a subphrenic abscess, which was aspirated, permitting air to enter the space. Note the elevation of the diaphragm on this side.

The differential diagnosis between perforated peptic ulcer and appendicitis is not always easy because the irritating gastric fluid gravitates downward and to the right, due to the position of the mesentery. A careful history, the boardlike rigidity, and the free air demonstrable by x-ray will in most instances clear up the diagnosis. Some acute perforations heal over or seal themselves by attachment to the gall bladder or omentum.

Hemorrhage and perforation do not often occur together. Such cases have been reported but as a rule acute perforations do not occur in bleeding ulcers and bleeding does not occur in acute perforating ulcers. This is not true of the chronic variety where perforation occurs on the posterior wall in a slow manner.

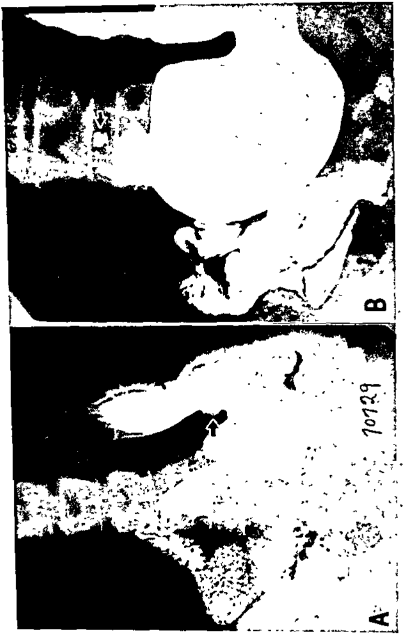

Fig. 279.—*A*. Gastric ulcer on the lesser curvature just above the incisura. Arrow points to crater. *B*. Duodenal ulcer with obstruction due to scarring and spasm. Arrow points to crater. Note the huge dilatation of the stomach.

Obstruction may occur at the pylorus (pyloric stenosis) and less commonly higher up in the stomach as an hourglass contraction. The obstruction is the result of fibrosis caused by the healed or healing ulcer. This scar may be very thick and as it contracts stenosis occurs. This incomplete obstruction causes a hypertrophy of the stomach wall. As the

pylorus becomes more and more occluded, the stomach wall gradually dilates and becomes thin and atonic.

Carcinoma secondary to ulcer occurs in about 5 to 10 per cent of *gastric ulcers.* This is seen mostly in those ulcers which have a fairly low acid and are on the greater curvature. The fact that 3 to 5 per cent of all cancers of the stomach start out with a diagnosis of ulcer does not prove the relationship, because such ulcers may be ulcerating carcinomas from the start. This relationship of cancer and ulcer is not seen on the duodenal side, although cancer of the duodenum exclusive of ampullary carcinoma does occur in the presence of ulcer scars.

Most ulcers heal with a soft scar or slight puckering, and these are commonly encountered at operation, even after severe hemorrhage which occurred only two to three weeks before surgery. Many ulcers go through stages of quiescence and exacerbation, much like varicose ulcers which are treated by bed rest until they heal and which form again when the patient is back at work.

Symptoms and Signs.—Peptic ulcer is a disease of young adults, usually males, but during World War II the incidence rose greatly in females. Since then the male predominance is again evident. Is this another evidence of "stress and strain" as a cause? Children from birth to 7 years of age have ulcers more of the acute type. We have seen two with hemorrhage following spinal fusions and one with perforation without apparent cause. Between 7 and 15 years the ulcer resembles more the chronic type.

Pain or *gnawing* sensation which appears shortly after eating (gastric ulcer) or about two hours after (duodenal ulcer) and which is usually relieved by food is the most constant symptom. This has led to the "pain-food-relief" triad used in describing ulcer pain. Alkalis also give relief.

Pain in ulcer may be due to an increased sensitivity of the nerve endings which changes the distress of normal hunger contraction to severe hunger pains; peristalsis, or local spasm, occurring at the site of the ulcer in muscle of changed sensitivity; and, perhaps most important, chemical irritation by the hydrochloric acid.

Pathways of pain are probably by way of the visceral splanchnic nerves; however, the varying shifts of pain into different regions is due to involvement of other organs, and the parietal peritoneum and mesentery which in turn send their impulses over cerebrospinal nerve twigs (spinal-sensory-somatic pathway). Therefore, the referred pain will be over the course of the spinal nerve involved. Perforating posterior duodenal ulcers produce referred pain to the right upper quadrant and right side of back, whereas perforating gastric ulcers produce pain in the left upper quadrant and left side of back. Perforating lesions involving the diaphragm are painful, and the pain is referred to the shoulder. This is explained by the assumption that the painful impulses reach the spinal cord over the phrenic nerve which arises from the fourth cervical seg-

ment (also to some extent from the third and fifth cervical); after going through the thorax, it supplies motor fibers to the diaphragm and sensory fibers to the diaphragmatic pleura as well as the peritoneum lining the undersurface of the diaphragm. Since the supraclavicular, suprascapular, and supra-acromial nerves arise in the same spinal cord segment, pain is referred to the shoulder. This same mechanism explains the shoulder pain in a perforated ulcer with air and acid chyme under the diaphragm, also any diaphragmatic irritation.

The pain of ulcer is not a pain in the sense that morphine is required. It is an uneasiness relieved by pressure in the epigastrium momentarily. The pain is not constant. It varies with seasons, time of day, degree of work, mental strain, preoccupation, lack of rapport. Night pain is uncommon unless there is obstruction or carcinoma. The diagnosis is made from the symptoms but is confirmed by a barium meal fluoroscopic examination.

Hemorrhage relieves all symptoms of ulcer for a while. If large and from the stomach, there is apt to be hematemesis as well as "coffee ground" vomitus and tarry stools; if from the duodenum, no evidence of bleeding is seen until the black tarry stool appears. Only 75 c.c. of blood are required to produce a tarry stool, and the test for occult blood will be present for three to four days afterward.

An increase in blood urea nitrogen occurs following alimentary absorption of large amounts of digested protein. This condition occurs clinically most often in patients with bleeding peptic ulcer. In either, symptoms of shock appear early, but they are transient and mild, consisting of simple fainting. Within six to eight hours blood changes begin to occur due to hemodilution. In milder types of bleeding no symptoms occur. It is astounding to see patients walk into the office with blood counts of 1 to 2 million and hemoglobin as low as 5 Gm. The diagnosis is made from the anamnesis and symptoms and signs. Other causes of bleeding must be ruled out.

Acute perforation is usually sudden and dramatic. The pain is excruciating, but there is no shock early unless a very large hole is present and a full stomach has flooded the peritoneal cavity. Vomiting is usually absent. The pain at first is in the epigastrium but may be in the upper right quadrant and right shoulder. Later (two to three hours) the pain may be in the right lower quadrant. This is thought to be due to the direction of the small bowel mesentery which guides the gastric contents into this area. This often makes the differential diagnosis between acute perforated appendicitis and ruptured ulcer difficult. Usually the pain is so severe that it is mimicked by only a few other calamities. One of these is acute hemorrhagic pancreatitis which occurs usually in very heavy men after they have eaten a large meal or drunk much alcohol and have exerted themselves by strenuous work, yet the identical circumstances may surround a perforated ulcer, and if the

perforation is in the lesser peritoneal sac, the picture is almost identical. Mesenteric thrombosis resembles a ruptured ulcer insofar as pain is concerned, and, if high up, may cause bright red bleeding resembling a bleeding ulcer. Usually the vomitus is dark, and there may be blood in the stools if the inferior mesenteric is occluded. A scout film of the abdomen may reveal gas under the diaphragm in the upright position and on the lateral wall of the abdomen if the x-ray is taken in the lateral decubitus position. Gas in the stomach is decreased, but even so the magenblase prevents a clear delineation of free air which is better observed over the liver. Formes frustes types and chronic perforation cause pain which is milder and is referred to various sites, depending on the location of the perforation.

Obstruction causes continual pain and fullness with eructation of sour fetid material. Later, vomiting occurs which may be prodigious. Sometimes food eaten twenty-four to forty-eight hours previously is vomited. Fluoroscope examination with barium shows gastric retention above the level of the perforation.

Carcinoma in an ulcer of the stomach is to be suspected in middle-aged or older people who complain of loss of appetite, strength, and weight. They have low or absent acidity (though this is not invariable) and an anemia which persists, and their pain is present in the morning on arising and is not relieved by food but may be aggravated by it. Barium meal and fluoroscopy help materially, but in carcinomas which grow centrifugally, the x-ray findings are notoriously misleading. Ulcer patients have a good appetite, higher than normal acidity (not invariable), and normal blood count (unless there has been persistent bleeding).

Treatment.—The treatment is usually nonsurgical and consists of a bland diet with frequent feeding, especially milk and cream. Cream and milk tend to inhibit gastric secretion, cause the expulsion of bile from the gall bladder (in the case of cream), and stimulate pancreatic secretion. They thus reduce acidity by direct action, and also by indirect action by neutralization of the acid. Also by the fact that fat in the intestine releases enterogastrone which inhibits gastric secretion. The rationale for this is that these foods act much as a sponge, sopping up the free hydrochloric acid and thereby preventing it from eroding the mucous membrane. Often alkaline powders, such as calcium carbonate, magnesium oxide, and bicarbonate of soda, are used. Frequently the latter has been tried by the patient before consulting a physician. Sodium bicarbonate, if used to excess, causes a state of alkalosis, with gastric tetany, and it has an irritant action on the gastric mucous membrane.

Other forms of medical treatment include dietary measures first introduced by Celsus (about 10 A.D.), who advocated "a soft smooth diet without acid or acrid substances and light wine to be not too hot or too

cold." Liberal diets adequate in minerals, vitamins, and protein are best. Timing is important, and the bland meal, together with 10 A.M., 3 P.M., and 10 P.M. feedings, is designed to sop up excess acid. The continuous milk and cream drip is designed to accomplish the same purpose. Diets should not include condiments and roughage. Duodenal feeding through the Einhorn tube has been employed to put the stomach at rest. Amino acids have been advocated because these mixtures are antacid and easily assimilable so that hypoproteinemia may be combated. Alkalis and adsorbers are advised by some, condemned by others. Among these are calcium carbonate, the aluminum compounds such as aluminum hydroxide gel, and magnesium oxide.

"Enterogastrone" has been used intramuscularly by day in the treatment of recurrent ulcer. Other drugs such as atropine are used to cut down vagus stimulation, hypermotility, hypertonicity, and hypersecretion, and phenobarbital for sedation.

Recurrences are common (80 to 85 per cent) after medical treatment, but surgery is indicated only in the intractable types, especially on the posterior side; persistent gastric ulcer or one or more of the complications, namely, hemorrhage, perforation, obstruction, chronicity and intractability due to erosion into the pancreas or chronic perforation with diverticulum-like protrusion, chronic gastric ulcers which may be carcinomas, and very large ulcers.

Surgical treatment is designed to relieve pain, reduce the acid, or produce anacidity, provide for neutralization of the remaining acid by reflux of alkaline juices and mucin, relieve obstruction, and remove the ulcer on the gastric side and also duodenal side if possible. To accomplish these objectives, almost every conceivable operation has been tried. These may be divided into the following groups:

1. Pyloroplasties: Heineke-Mikulicz, Horsley's, Finney.

2. Gastrojejunostomy and gastroduodenostomy with stomach intact anterior to transverse colon or posterior. Devine exclusion. Fensterer antral exclusion with excision of antral mucosa and without excision of this mucosa which is supposed to contain the hormone which stimulates gastric secretion.

3. Combinations of 1 and 2. Duodenogastric intussusception with posterior gastrojejunostomy, Devine and Fensterer exclusions. (See Fig. 280.)

4. Removal of portions of the stomach. Pylorectomy, antrumectomy, partial gastrectomy, subtotal gastrectomy, fundusectomy, sleeve resection, or segmental gastrectomy. (See Fig. 281.)

The operations in 4 are subdivided according to the manner in which the continuity of the intestinal canal is re-established. (1) In sleeve resections the stomach itself is sutured—gastrogastrostomy; (2) in all others, the stomach is anastomosed to the duodenum in accordance with Billroth I gastroduodenostomy (Billroth I, Kocher, Schoemaker, Von Haberer-Finney, Horsley, von Haberer) or to the jejunum like a

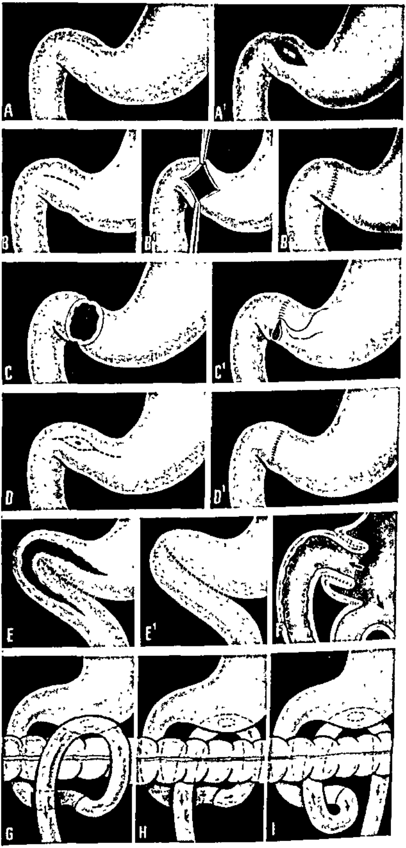

Fig. 280.—See opposite page for legend.

Billroth II gastrojejunostomy (Billroth II, von Eiselsberg, Polya, Hofmeister-Finsterer, Moynihan, Polya-Balfour or anterior Polya) (see Fig. 282).

5. Denervation by parasympathectomy or vagotomy, supradiaphragmatic and infradiaphragmatic, transthoracic vagotomy, or transabdominal vagotomy, respectively. (See Fig. 283.)

Denervation with gastroenterostomy or resection. Sympathetic denervation by left splanchnicectomy and celiac ganglionectomy or bilateral splanchnicectomy. Combined vagotomy and splanchnicectomy.

The merits and demerits of the various operations have been discussed in volumes of writings, and the results have been investigated experimentally and clinically. There is no operation which guarantees against recurrence, and even the most radical, consisting of a resection of 75 per cent of the stomach with short afferent loop, is followed by recurrences. Less radical subtotal resections have a recurrence rate of 5 to 10 per cent. At present, in our opinion, the following conclusions may be drawn concerning the *indications* and *reasons* for the particular operation selected and *complications* which may follow its use:

1. Pyloroplasty is used only rarely in the treatment of ulcer. In older individuals with low acid and obstruction due to a fibrosed *duodenal* ulcer which is "burned out" or inactive, a pyloroplasty of the Finney type is indicated. This is especially true in badly debilitated

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Fig. 280.—Operations upon the stomach without resection. Stomach operations are very numerous and are done in so many different ways that in this and the succeeding diagrams of various types of operations only the more commonly practiced varieties will be illustrated.

In general, operations upon the stomach are divided into three large classes: first, those which are done upon the outlet and the inlet of the stomach without removing any portion thereof; second, operations upon the stomach with removal of a part or all of the organ; and third, those operations which are done outside the stomach and which deal with the nervous innervation of the stomach. In this figure the diagrams represent various types of surgical procedures upon the pylorus and the body of the stomach without resection. *A*, Rammstedt-Fredet. This operation consists of incising down to the mucous coat in a longitudinal manner, then spreading the muscle which is hypertrophied as a rule and allowing the mucous membrane to bulge as shown in A^1. *B*, Heineke-Mikulicz pyloroplasty. This consists of dividing the pylorus longitudinally and suturing it transversely as shown in B^1 and B^2. *C*, The Judd pyloroplasty which consists of removing the anterior third of the pylorus and then suturing it transversely as shown in C^1. *D*, Horsley-Judd types of pyloroplasty. The Horsley type is a variation of the Judd variety and consists of excising the ulcer at the pylorus, carrying the incision in a longitudinal fashion proximally and distally, and then closing the pylorus in a transverse manner as depicted in D^1. *E*, Finney gastroduodenostomy or Finney pyloroplasty. This operation consists of suturing the duodenum to the greater curvature of the stomach, and then by a horseshoe incision the stomach and duodenum are brought together as shown in E^1. This creates a wide opening from stomach to the duodenum and is useful in certain types of pyloric stenosis from ulcer where the risk of doing more radical procedures is too great or technically too difficult. *F*, Duodenogastric intussusception with posterior gastrojejunostomy. This operation is useful in those patients in whom more extensive procedures are dangerous, and yet gastrojejunostomy is risky because of the danger of jejunal ulcer or marginal ulcer. By this method Brunner's glands are brought up into the pyloric antrum, thereby tending to cause an increase in gastric mucin. This factor offers some protection to the stoma of the gastrojejunostomy against jejunal or marginal ulcer. The operation has also been useful in perforations where after covering the perforation the opening from the stomach to the duodenum has been so narrowed that it is feared that obstruction will ensue. *G*, Gastrojejunostomy. This is the anterior form and consists of bringing the jejunum to the anterior portion of the stomach as close to the greater curvature as possible and in front of the transverse colon. It was first done by Wolfer in 1881. The posterior gastrojejunostomy or, as it is sometimes called, gastroenterostomy was first done by Courvoisier in 1883. This type operation is very useful in all forms of benign obstruction. However, the danger is a recurrent ulceration at the site of the anastomosis so that the operation is not commonly employed today. *H*, Posterior gastrojejunostomy antiperistaltic; that is, from left to right. *I*, Posterior gastrojejunostomy isoperistaltic; that is, from right to left.

patients without a great amount of extrinsic adhesions and fixation. It is a simple safe operation with few complications but offers no protection against a recurrent ulcer.

2. A simple posterior gastroenterostomy is indicated under conditions outlined in 1 where great scarring of the pylorus prevents its use in anastomosis readily. The Devine exclusion operation has a place in massive hemorrhage in patients over 50 years of age, although it is apt to be followed by secondary hemorrhage unless a second operation may be done later. The chief complication is recurrent ulcer or jejunal ulcer. Not infrequently a gastrojejunocolic fistula may form, causing diarrhea, vomiting, pain, loss of weight, and even death from starvation and dehydration. The treatment of this complication requires excision of the ulcer and reestablishment of the normal preoperative status. If the patient can stand more or if pyloric obstruction makes further surgery mandatory, gastric resection is done at the same time. This may be deferred for a second stage by doing an enterostomy for feeding when

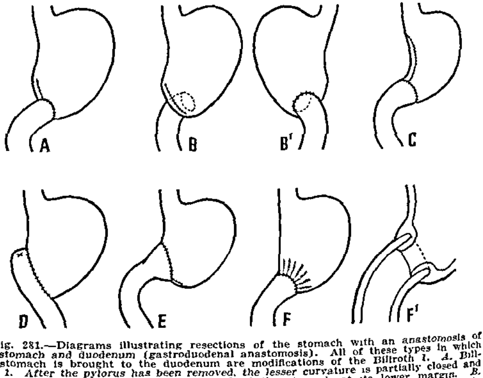


Fig. 281.—Diagrams illustrating resections of the stomach with an *anastomosis* of the *stomach* and duodenum (gastroduodenal anastomosis). All of these types in which the stomach is brought to the duodenum are modifications of the Billroth I. *A.* Billroth I. *After the pylorus has been removed, the lesser* curvature is partially closed and the duodenum is sutured to the open end of the stomach at its lower margin. *B.* Kocher. In this case the distal end *of the stomach is* closed and the duodenum is brought up to the posterior margin of the closed stomach. *B*[1]. Posterior view showing the end of the duodenum anastomosed to the stomach. *C.* Schoemaker. In this instance the lesser curvature of the stomach is sutured and brought down to the same size as the duodenum and then an end-to-end anastomosis *is done. D.* Von Haberer-Finney type. In this operation the side of the duodenum is brought up to the end of the stomach so that the entire end of the stomach is open. *E. Horsley.* The Horsley type of gastroduodenal anastomosis uses the lesser curvature end of the stomach to suture to the duodenum and closes the greater curvature end. *F. Van Haberer.* A *modification of the* operation shown in *D.* The stomach is, so to speak, narrowed or puckered so that it fits the end of the duodenum. A modification of *this has* been done by some *in the following* way. *The* duodenum is split longitudinally and its ends are flared open so that the opening will be large enough to fit the open end of *the stomach.* *F*[1]. Another *modification of von Haberer gastroduodenostomy.* The stomach wall is folded over on the invaginated duodenum.

obstruction demands this. Rarely, parts of the jejunum and transverse colon must be removed and anastomosed.

Finsterer exclusion with mucosa intact is useful where there is great inflammatory reaction and inversion of the duodenal stump is difficult. This may be followed by recurrence, and therefore at a second stage the remaining antrum and ulcer with duodenal cuff may be removed.

The greatest danger of complication in duodenal closure and gastrojejunostomy lies in leakage from the duodenal stump. This may be due to anomalies in the blood supply (gastroduodenal, supraduodenal right gastric, right gastroepiploic, and superior pancreatico-duodenal) which may cause necrosis when principal branches are tied. Often it is necessary to bury the duodenal stump in the pancreas or close it with an attached omental graft or a free graft of the omentum.

The Finsterer operation with mucosal excision gives better results and is useful in a densely adherent pylorus or a poor-risk patient. The results are as good, when combined with adequate stomach resection, as any other type of operation.

3. Combinations of 1 and 2. Poor risk patients who are confirmed "ulcer formers," as evidenced by previous perforated ulcers, recurrence on dietary management, and after vagotomy, may be benefited by duodenogastric intussusception combined with posterior gastroenterostomy. This combination has been used by us with encouraging results. Its value lies in the fact that it moves the pylorus and first portion of the duodenum into the pyloric antrum. The ulcer-bearing area (the pyloric end of the stomach and the pars superior duodenum) is thereby transplanted into a new and more highly acid environment. The effects of this may be hypothetically explained in the light of modern gastric physiology: Acids are reduced because enterogastrone may be released in greater abundance, thereby reducing gastric secretion; the acid in the duodenum is greatly increased, thereby further reducing gastric secretion; and, above all, the transplanted mucin glands (Brunner's and pyloric glands) are stimulated, producing prodigious amounts of mucin. The objections to the operation as follows: the pyloric mucosa is left intact so that it may presumably stimulate secretion and the invagination is apt to delay emptying time. To offset the latter, the operation is combined with posterior gastroenterostomy so that the gastroenteric stoma is continuously bathed with mucin.

4. Of all the resections the most popular is a two-thirds to three-fourths gastrectomy with a Polya type anastomosis, using a short duodenojejunal loop. Wherever possible, the duodenal ulcer is included in the resection. If the ulcer is too close to the ampulla, it is left in situ, and if this cannot be accomplished because of dense adhesions, a two-thirds gastrectomy is done; the pylorus is left but its mucosa is removed. If the inflammatory reaction is too great for mucosal excision, the pylorus is left intact. Later it may be removed. Some have even

patients without a great amount of extrinsic adhesions and fixation. It is a simple safe operation with few complications but offers no protection against a recurrent ulcer.

2. A simple posterior gastroenterostomy is indicated under conditions outlined in 1 where great scarring of the pylorus prevents its use in anastomosis readily. The Devine exclusion operation has a place in massive hemorrhage in patients over 50 years of age, although it is apt to be followed by secondary hemorrhage unless a second operation may be done later. The chief complication is recurrent ulcer or jejunal ulcer. Not infrequently a gastrojejunocolic fistula may form, causing diarrhea, vomiting, pain, loss of weight, and even death from starvation and dehydration. The treatment of this complication requires excision of the ulcer and reestablishment of the normal preoperative status. If the patient can stand more or if pyloric obstruction makes further surgery mandatory, gastric resection is done at the same time. This may be deferred for a second stage by doing an enterostomy for feeding when

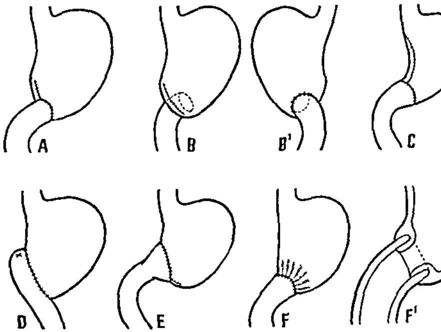


Fig. 281.—Diagrams illustrating resections of the stomach with an anastomosis of the stomach and duodenum (gastroduodenal anastomosis). All of these types in which the stomach is brought to the duodenum are modifications of the Billroth I. *A*. Billroth I. After the pylorus has been removed, the lesser curvature is partially closed and the duodenum is sutured to the open end of the stomach at its lower margin. *B*. Kocher. In this case the distal end of the stomach is closed and the duodenum is brought up to the posterior margin of the closed stomach. *B*¹. Posterior view showing the end of the duodenum anastomosed to the stomach. *C*. Schoemaker. In this instance the lesser curvature of the stomach is sutured and brought down to the same size as the duodenum and then an end-to-end anastomosis is done. *D*. Von Haberer-Finney type. In this operation the side of the duodenum is brought up to the end of the stomach so that the entire end of the stomach is open. *E*. Horsley. The Horsley type of gastroduodenal anastomosis uses the lesser curvature end of the stomach to suture to the duodenum and closes the greater curvature end. *F*. Van Haberer. A modification of the operation shown in *D*. The stomach is, so to speak, narrowed or puckered so that it fits the end of the duodenum. A modification of this has been done by some in the following way: The duodenum is split longitudinally and its ends are flared open so that the opening will be large enough to fit the open end of the stomach. *F*¹. Another modification of von Haberer gastroduodenostomy. The stomach wall is folded over on the invaginated duodenum.

advised two-thirds gastrectomy for high ulcers as a palliative measure since acids are greatly reduced. Here a transthoracic resection of the cardia would be more apropos. Statistics on the mortality of radical gastrectomy vary from 2 to 10 per cent.

Complications which may follow subtotal gastrectomy are (1) recurrent ulcer or gastritis, (2) dumping syndrome, (3) inability to regain weight, (4) anemia, (5) hyperglycemic and hypoglycemic syndromes, (6) rarely, duodenal fistula. From 20 to 30 per cent of all gastrectomized patients have some complaints.

Recurrent ulcer occurs in about 5 per cent; however, this figure varies greatly in different groups of statistics. Some patients complain of ulcerlike symptoms with occasional bleeding. These cases are acute ulcers or *small erosions* with *gastritis*. More than half of our patients fail to gain weight, regardless of rest or diet. Anemia is transient and readily controlled but is persistent in a very small group. Duodenal fistula is the result of leakage from the inverted duodenum as a rule. Unfortunately many fatalities are due to this leakage since drainage is not usually employed. The treatment of fistula is directed chiefly to the replacement of electrolytes lost. The fistula will usually close if the normal channel is open (see Chapter 5).

The Dumping Syndrome.—Gastrectomy was formerly done so that the stoma between the stomach and the jejunum was left so wide that large quantities of gastric material were suddenly dumped into the jejunum which was not capatious enough to hold it. This resulted in a syndrome which consisted chiefly of abdominal distention, cramplike pains, constipation, and rarely diarrhea. In addition, there were vague *symptoms of a sense of goneness, nausea, and fainting. This has largely* been corrected by modifying the Polya operation with the Hoffmeister technique, which consists of closing the lesser curvature portion of the stomach and anastomosing the jejunum to the greater curvature half.

III. *Open end of stomach. C.* Kronlein-Balfour. This is isoperistaltic, antecolic, and end-to-side. The entire end of the stomach is anastomosed to the side of the jejunum. *C*[1], Moynihan II. This is an antiperistaltic, antecolic end-to-side gastrojejunostomy, in other words, the jejunum is brought up anterior to the transverse colon, the entire end of the stomach is sutured to the side of the jejunum, but the flow of the current is from greater to lesser curvature, thereby creating an antiperistaltic effect. *C*[2], Reichel-Polya. This is an isoperistaltic (that is, from lesser to greater curvature), retrocolic, end-to-side gastrojejunostomy. This is one of the most common varieties employed today following a subtotal gastrectomy.

IV. The stomach is not resected. These operations are known as the exclusion operations. *D.* The stomach is divided, the distal portion is turned in, the proximal portion is brought up to the jejunum, usually according to the Reichel-Polya or Kronlein-Balfour type of end-to-side anastomosis. However, any of the varieties of anastomosis of gastrojejunostomy may be practiced. The exclusion operation is rarely done except in those cases where the inflammatory process is too acute and the patient too sick to permit any further type of surgery. Later the antrum may be resected. A modification of this is the one advocated by Finsterer in which, in addition to excluding the antrum, he takes out the mucous membrane of the antral portion which is supposed to secrete the acid-producing hormone. These have been known as the Devine exclusion and the Finsterer antral exclusion with and without resection of the antral mucosa. *E.* The Roux type. This is also known as the "En-y" type of anastomosis. Here the jejunum is severed, the distal limb is sutured to the cut end of the stoma of the stomach or to the side of the stomach as in Billroth 2, and the proximal limb is sutured to the side of the distal jejunum. This operation is useful where there is an insufficient amount of bowel to bring up to the stomach or where this is technically not possible because of dense adhesions. This type of anastomosis avoids viscious circles and dumping syndromes which have been described in connection with other types of operations.

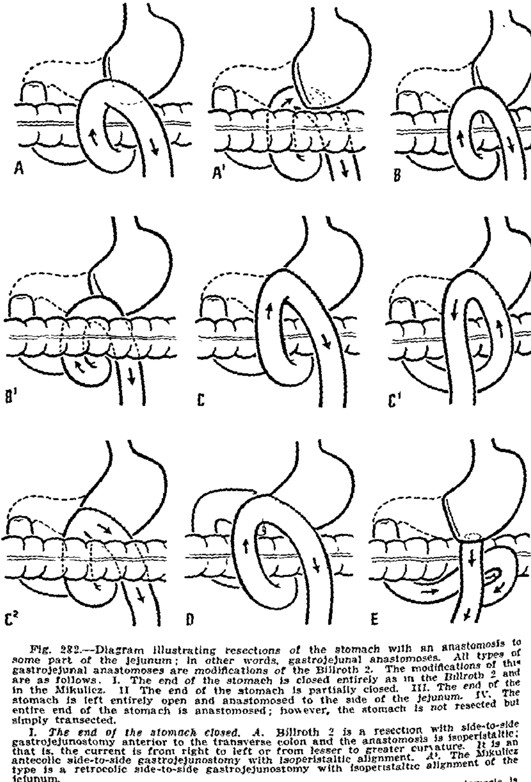


Fig. 282.—Diagram illustrating resections of the stomach with an anastomosis to some part of the jejunum; in other words, gastrojejunal anastomoses. All types of gastrojejunal anastomoses are modifications of the Billroth 2. The modifications of this are as follows. I. The end of the stomach is closed entirely as in the Billroth 2 and in the Mikulicz. II The end of the stomach is partially closed. III. The end of the stomach is left entirely open and anastomosed to the side of the jejunum. IV. The entire end of the stomach is anastomosed; however, the stomach is not resected but simply transected.

I. *The end of the stomach closed.* A. Billroth 2 is a resection with side-to-side gastrojejunostomy anterior to the transverse colon and the anastomosis is isoperistaltic; that is, the current is from right to left or from lesser to greater curvature. It is an antecolic side-to-side gastrojejunostomy with isoperistaltic alignment. A¹. The Mikulicz type is a retrocolic side-to-side gastrojejunostomy with isoperistaltic alignment of the jejunum.

II. *Partially closed end of the stomach.* B. Von Eiselsberg. The anastomosis is antecolic end-to-side, isoperistaltic, but the superior portion of the stomach is closed for a greater part of its surface, thereby creating a small stoma. This allows resection of a greater portion of the lesser curvature and decreases the size of the stoma, thereby tending to avoid the so-called dumping syndrome. B¹. Hoffmeister-Finsterer. This is a retrocolic, end-to-side gastrojejunostomy and is isoperistaltic; that is, from lesser to greater curvature just as the von Eiselsberg's type.

(Continued on opposite page)

follows gastroenterostomy operations. In the hypoglycemic phase, Evansen, whose work was a pioneer study in this field, shows that blood sugars will fall to 65 mm. or less.

Vagotomy Treatment of Gastroduodenal Ulcer.—Recently, due to the studies of Dragstedt and co-workers, the operation of vagotomy has been reintroduced. Dragstedt isolated the stomach in dogs and introduced a gold-plated cannula, leaving the blood supply intact as well as the vagus innervation. Such stomachs are found to secrete an average of 100 c.c. of gastric juice with a free hydrochloric acid concentration of .35 to .42 per cent in twenty-four hours. The total secretion for a month was collected, and then the vagus nerves were divided in the chest just above the diaphragm. The volume of gastric juice immediately declined to an average of 410 c.c., with a free acidity of 0.11 to 0.32 per cent, and this effect persisted for at least sixty days. The operation was found to have no effect on the secretory responses of the stomach to histamine or caffeine, but it abolished the stimulating effect of insulin hypoglycemia. Following this experimental work, Dragstedt began doing the operation of vagotomy through the transthoracic route. The vagus was divided and the proximal ends were tied and buried in the mediastinal pleura so that the two ends could not reunite. Later the operation was performed through an abdominal approach so that conditions in the abdomen could be carefully investigated.

Dragstedt has employed the insulin test to determine if all of the vagus secretory fibers to the stomach were interrupted. The insulin test is as follows: After aspirating the fasting contents of the stomach with a Luer syringe, a sample of blood is taken for the determination of fasting glucose; then 15 units of insulin are injected intravenously and the time of the injection noted. If severe symptoms of hypoglycemia develop, sterile glucose solution is given intravenously. For two hours after injection the stomach contents are aspirated every fifteen minutes and the volume, time of aspiration, and presence of mucus or bile are recorded. A sample is kept for acidity titration. Usually the minimum blood sugar value is reached within thirty minutes. If all of the vagus fibers have been cut, there will be no rise in acidity. This test is usually performed two weeks after the operation. Theoretically, if gastric secretion is decreased, so is mucin. Even though acid has been reduced by vagotomy, we are not sure that this is the entire factor in the causation of ulcer and, if it is, at the same time we are reducing the normal protecting mechanism of the gastric mucous membrane, mucin, so that what little acid remains may do harm.

Clinical Evaluation of Vagotomy.—The results of vagotomy according to Dragstedt have been very good. There are, however, certain complications which are inherently present in the operation. The first is a decrease in the motility of the stomach to such a degree that not infrequently a posterior gastroenterostomy has to be done in order to permit

In addition to the dumping syndrome, another group of symptoms may occur consisting of the following: mild or severe sensations of warmth, sweating, dizziness, faintness, palpitation, nausea, and abdominal pain. In extreme instances there may be syncope or convulsions.

The first group of symptoms occur shortly after the ingestion of food; the other after a latent period of one hour or longer. Rarely the two groups of symptoms may appear in the same individual. It is thought now that both types are related to the rate of absorption of sugar from the small intestine into the blood stream. When the large volume of the stomach content suddenly pours into the unprepared jejunum, a transient hyperglycemia results. This elevated blood sugar is tolerated well by many patients. In a few, however, some symptoms arise. In a study of these patients it has been found that symptoms sometimes precede the rise of blood sugar which does occur as a result of the abnormally quick absorption. Previously it has been thought that the early symptoms following the ingestion of food were due to the dumping syndrome. However, experimental work with balloons showed that this is not the entire explanation. Whatever the exact mechanism, there is in most instances an increased gastric motility and an abnormally rapid delivery of food into the jejunum, usually aided by a short circuit around the duodenum. There is further a failure of normal dilution of hypertonic solutions of sugar in the stomach because of the first two factors mentioned.

Fourth, there is an abnormally rapid absorption of sugar from the jejunum as a result of hypertonic solutions and a larger delivery of food than normal. Fifth, possible effects of distention of the jejunum by direct irritation of the mucosa by undiluted food and the susceptibility of the individual patient. It is perhaps correct to assume that the hyperglycemia phase does not play an important role in the causation of postgastrectomy symptoms which occur two to three hours after eating. Hypoglycemia may account for some of the symptoms which occur in the early morning before the intake of food. The hypoglycemic phase can be partially abolished by the use of atropine and by frequent feedings, especially if atropine is given before bedtime.

Apparently the vagus plays no role in these postgastrectomy symptoms. The entire syndrome is due to a very large absorption of sugar in a very short period of time. Patients often have a blood sugar of 250 to 400 mg. per 100 c.c. of blood. This calls forth a large amount of insulin. The most likely explanation for the syndrome just described is that of a hypoglycemia, not unlike that produced by too much insulin.

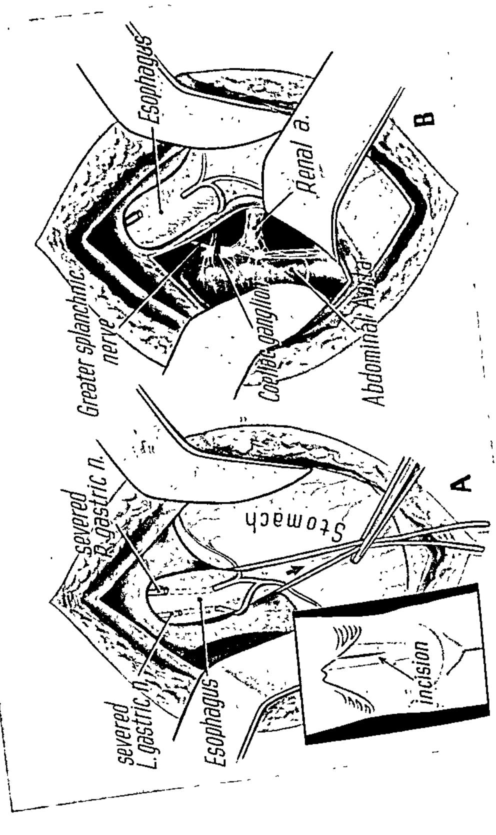
The treatment for this syndrome is simple. Patients usually learn the trick of eating solids at the beginning of the meal, so that they will leave slowly, and of restricting their sugar intake. Frequent feedings also help the condition by keeping up a constant level of blood sugar. The foregoing symptoms are not limited to postgastrectomy but also

Fig. 283.—Vagotomy. Operations recently attempted to ameliorate gastric and duodenal ulcer have been directed against the nerve supply of the stomach. Denervations of the stomach are not new but have recently been revived. At present the operation of vagotomy offers great promise. This may be done through an abdominal approach and requires the division of both anterior and posterior vagus nerves. In addition, some type of anastomosis is done to provide for the emptying of the stomach which becomes atonic. For this purpose a posterior gastrojejunostomy is usually employed. The transabdominal approach further offers the surgeon the opportunity to investigate the local condition and decide on what operation is best suited for the particular state of affairs. The transthoracic type of vagotomy is, perhaps, better insofar as it can remove more completely the vagus nerve and its branches. However, gastric atony may ensue. For this, the drug urocholine is sometimes employed. In general if an operation has previously been performed on the stomach and there is a recurrence of the ulcer, transthoracic vagotomy may be a useful procedure. If no previous surgery has been attempted, the transabdominal approach is to be preferred.

Bilateral splanchnicectomy has also been suggested for the treatment of peptic ulcer. The combined vagotomy and left splanchnic interruption has also been tried.

A. Vagotomy through a transabdominal approach. The left lateral hepatic ligament is divided to permit retraction of the left lobe of the liver. The peritoneum over the esophagus is divided transversely and the esophagus is gently pulled downward with the aid of a piece of umbilical tape.

B. Division and excision of a portion of the left splanchnic and celiac ganglion through an incision in the gastrohepatic ligament.


Esophagus
Renal a.
B
Greater splanchnic nerve
Coeliac ganglion
Abdominal Aorta
severed R. gastric n.
Stomach
A
severed L. gastric n.
Esophagus
incision

sympathetics and, therefore, if they are divided, there should result a decrease in painful stimuli which may originate in the stomach. As we have pointed out under the subject of motor activity of the stomach, this operation on theoretical grounds could be effective because division of the splanchnics together with the removal of the celiac ganglion, particularly the left, might result in increased mobility or relaxation of the cardia and pylorus and relief from pain. The contention that "no acid, no ulcer" would seem to contraindicate the operation because division of the splanchnics definitely does not decrease the volume or the degree of acidity of the gastric juice. The left splanchnic and left celiac ganglion form the gastric and esophageal plexuses and, therefore, it is probably true that only the left nerve and ganglion need be excised.

The advocates of complete denervation believe that both vagotomy and splanchnicectomy and celiac ganglionectomy would result in an ideal state so far as the production of ulcer is concerned. Here again we would have the decrease in gastric juice together with the obviation of the bad effects of vagotomy. The combined procedure has been done in too few cases up to the present to evaluate the operation clinically. However, in those which we have observed the results were comparable to those of vagotomy, and in one case a recurrence took place. Here, again, complete denervation of the stomach is probably temporary. The intrinsic nervous mechanism of the stomach ultimately reasserts itself. These operations must await further study before they can be definitely evaluated.

The Treatment of Complications of Gastroduodenal Ulcer.—(1) For a long time the dictum of treating *hemorrhage* from gastric or duodenal ulcer was to sit by the bedside and observe the patient in shock, hoping that the factors involved in the natural arrest of hemorrhage would take place and that the patient would soon perform a spontaneous arrest. In addition, small transfusions were given with the idea that with a large one, it would increase the blood volume to such a degree that hemorrhage would recur. The same was said concerning intravenous fluids of all types. This dictum is good insofar as it takes care of the loss of blood volume and the electrolytes. However, it is probably erroneous in some ways. First of all, there was a great difference of opinion at that time as to whether or not any feeding should be given. One school of thought was that the patient should get nothing by mouth at all; another advocated the use of antacids, but no food; and a third used bland feedings to sop up the gastric juice. These three schools of thought were frequently arguing the merits and demerits of their respective methods of management. We can easily understand that food might dislodge a clot within a vessel. Our experience and that of other observers has shown that hemorrhage is not always spontaneously arrested in bleeding gastric or duodenal ulcers.

Studies of large series of bleeding ulcers show that a mortality of approximately 6 to 8 per cent, irrespective of age, takes place. In the

evacuation of the food, although urocholine is useful in treating this complication. In some patients there is diarrhea; however, this is not persistent. Practically all patients say they are relieved from pain caused by the ulcer. Recently, Dragstedt has used the transabdominal approach because it is difficult to know exactly the conditions within the stomach and duodenum. For example, the degree of obstruction, the degree of penetration in the posterior wall, the epigastric and periduodenal adhesions all had to be determined by x-ray and this was not entirely satisfactory. By doing the operation through the abdomen, if other operations are necessary in addition to vagotomy, they may be done at the same time. There is much to be said in favor of this operation. However, the work is too recent to evaluate it correctly, and hypothetically it may be assumed that whereas the section of vagus nerves will give temporary relief, the intrinsic nervous mechanism of the stomach will certainly reassert itself within a definite period of time, the length of which is not yet known. If the motor function of the vagus returns through reinnervation or through the intrinsic motor fibers within the stomach, then surely the secretory fibers will also become reinnervated, either through local channels or those closely related. However, much remains to be seen because the operation in its newer phase is relatively recent, and the final results cannot be estimated yet. There is a place, however, where vagotomy seems to be definitely indicated, and that is in patients who have had a gastrectomy and have had gastrojejunal ulcer or recurrence of ulceration. Here the local factors are known. The stoma is open, the stomach has been resected, and now there is a recurrent ulcer. In such patients a transthoracic vagotomy would certainly be indicated. If the night secretion on the empty stomach is an important factor in the causation of ulcer and the recurrence of ulcer, vagotomy would have a definite place. This seems to be the case in many instances. However, one wonders whether or not large doses of atropine might not accomplish the same thing. In our experience, this has not been true. Even with enormous doses of atropine, motility is decreased but little, and secretions are only slightly reduced. One last point should be made, and that is that the operation probably has no place in the treatment of *gastric* ulcer in which the problem of carcinoma is always present. For this type of ulcer certainly if vagotomy is used, resection should be done at the same time. Factors in favor of the operation are its relative ease of performance and its low mortality rate.

Clinical Evaluation of Splanchnicectomy and Celiac Ganglionectomy.—The operation of denervation of the sympathetics has recently been advocated based upon the fact that excessive activity of the sympathetics might conceivably lead to spasm of the cardia, atony of the fundus and body, and spasm of the pylorus sphincter. Apparently no change in secretion of gastric juice will result, but there should be vasoconstriction of the stomach. Apparently sensory nerve fibers run with the

follows; failure to improve promptly under a strict regimen of bed rest, moderate doses of morphine, milk and cream, 4 ounces, every two hours by mouth, adequate blood transfusions. If, under these conditions, there is recurrence of hemorrhage while the patient is on this strict regimen, then operation will save a life, and it should be done within twenty-four to forty-eight hours from the onset of the bleeding. The mortality in this group of patients will be lower than in those who are left without surgery. Although the most conservative operation which is possible and consistent with the condition of the patient should be done, yet simple ligations of vessels transduodenally or ligation of the gastroduodenal artery has not been found to be effective in arresting the hemorrhage permanently. Hemorrhage may occur from the inferior pancreaticoduodenal or even anomalous vessels. The operation of gastrectomy should be done if at all possible. If not, it should be done as soon as feasible.

Our greatest disappointments have been in patients who have been bleeding for ten days to two weeks or longer, having spurts of severe bleeding and then amelioration with recurrence of bleeding, treated by repeated blood transfusions. These patients stand surgery poorly. (See Chapter 13.) This is due to the fact that irreversible changes take place in tissue cells due to anemic anoxemia which definitely impede their reparative powers so that complications are frequent. Sutures will not hold, and infections due to leakage in the peritoneal cavity may occur. Therefore, it is best to perform the operations for arrestment of hemorrhage early or, if it has been decided that this is not indicated in the older group, then perhaps a feeding jejunostomy would be the treatment of choice, hoping for spontaneous arrest of the bleeding. In those patients who are on the borderline between acceptable risks for gastric surgery and treatment by palliation only, a simple operation should be done such as transduodenal suture of the bleeding ulcer or the use of Gelfoam sewn in place over the bleeding site simply as a temporary measure. A secondary operation should be done later, when the patient has had a chance to recover.

The Treatment of Perforation.—We have seen that ulcers will perforate anteriorly into the peritoneal cavity or posteriorly into the pancreas. We have also noted that the symptoms in these two lesions is entirely different. Rivers has recently suggested that perforation into the pancreas may be diagnosed by the symptoms and signs. He speaks of a clear-cut pattern of the visceral syndrome being distorted by the addition or the substitution of the somatic syndrome. The symptoms become more severe and frequently require more heavy use of opiates; relief obtained by the ingestion of food or alkalis is completely lacking, and there are periods of freedom from symptoms, with changes in location and extension of pain. The pain is usually through to the back in a fixed area over the upper lumbar vertebrae, but it may radiate in various directions in the

older group the mortality is much higher, ranging up to 20 per cent, and in those who have an initial severe hemorrhage, the mortality rate may even reach 30 per cent. Patients under 45 years of age with severe hemorrhage usually recover. Furthermore, in younger people, several hemorrhages may occur without any mortality. In older people a second hemorrhage may be fatal. In striking contrast to these statistics has been a recent study concerning the mortality rate of patients treated by gastric resection who are actively bleeding. The mortality rate has been reduced to a total of approximately 22 per cent. Among patients past

Fig. 284.—X-ray after barium meal showing great dilatation of the duodenum and stomach. This patient had a duodenal ulcer with extremely high acidity. Posterior gastroenterostomy had previously been performed. Incomplete obstruction resulted at the point of anastomosis. At operation a jejunal ulcer was found. The anastomosis was abolished and partial gastrectomy was done.

45 years of age with severe hemorrhage, the mortality rate was 42 per cent, and among those under 45 who had resection, the mortality rate was 30 per cent. According to these studies, patients under 45 years of age do not need surgery, as a rule, because the mortality is practically nil with conservative treatment. It is also true that patients past 45 years of age may have repeated hemorrhages without a fatality. It has been our rule to try to differentiate between patients with fatal and nonfatal types of hemorrhage, and the most consistent criteria have been as

stomach kept empty for a period of seven to ten days. Feedings are allowed, but the suction is started again in two to three hours after the feeding. Adequate fluid balance is maintained by intravenous injection, and plasma and blood volume is maintained by transfusion of plasma and whole blood. After the stomach has been lavaged and prepared in this manner, operation is performed. Usually this will consist in a subtotal gastrectomy. However, as has been pointed out, the indications for different types of procedures, such as duodenogastric intussusception, pyloroplasty, gastroenterostomy, may have their indications.

Carcinoma of the Stomach as a Complication.—Carcinoma of the stomach as a complication of ulcer is not usually determined until the time of operation. One statement should be made in connection with this complication at this time. The surgeon may hold the lesion in his hand and yet not be able to differentiate correctly between a chronic ulcer and a carcinoma or an ulcerating carcinoma of the stomach in its early phase. The size, the location, the friability are all equivocal factors. Therefore, the only sure test is microscopic examination. It is our custom, therefore, in all gastric ulcers to have a microscopic examination made by frozen section at the time of surgery. The ulcer on the duodenal side is usually free from the threat of carcinoma; however, this also should be examined after resection, or if this is not possible, a small piece of the border of the ulcer should be removed for biopsy if at all possible. If carcinoma has been discovered, radical resection, including the lymph nodes, should be done.

Neoplasms of the Stomach

Neoplasms of the stomach may be benign or malignant. Benign tumors of the stomach include (1) polyps and papillomas, (2) myoma, (3) fibromyoma, (4) adenoma. The rare forms of benign tumors of the stomach include fibroma, adenomyoma, lymphangioma, hemangioma, dermoid cysts, cyst adenoma and simple cysts, lipoma, and myxoma. Benign tumors of the stomach and duodenum, in contrast to the malignant ones, are extremely rare. Added to the list mentioned may be included neurofibroma and the granulomas of tuberculosis and syphilis. The latter, of course, are not true neoplasms except in that they may resemble the benign growths.

The importance of benign tumors is not only that of their symptoms and signs and discomforts but also of their potentialities. Chief among the latter tendency is that of obstruction. However, in the case of papillomas or polypoid tumors, the danger of carcinoma is inherent. Furthermore, the relationship between benign tumors and pernicious anemia may be closer than seems apparent. As a matter of fact, pernicious anemia is not infrequently associated with benign growths, although it must be said that the malignant types are more often the associated factor. The actual proportion of benign tumors to malignant ones is about 1 to 200, and they constitute approximately 1.3 per cent of all

abdomen. This type of perforation will require surgery, but this is not an emergency. In this discussion we are concerned with perforation into the free abdominal cavity, the symptoms of which have already been described. The perforation of a small ulcer, the so-called slow leak or formes frustes type, may be treated by conservative measures: the introduction of a Levine tube with suction and large doses of morphine, with nothing by mouth. This conservative treatment has not been universally accepted although good results have been reported. Most surgeons prefer immediate surgery, and the earlier this is performed, the less the chance for bacterial peritonitis and complications such as pelvic abscess, subphrenic abscess, and adynamic ileus. The operation should be the simplest which is consistent with closing the leak. This usually consists of a folding over of the anterior wall of the stomach, thereby closing over the hole. Large perforations require much overlapping of stomach wall as in duodeno-gastric intussusception. Since this may result in a narrowing of the pylorus, a complementary posterior gastrojejunostomy may be necessary. If this is not feasible because of the size of the perforation or because of the friability of the stomach wall, a large omental graft may be used which will adequately seal the opening. We have not encountered a case where we could not fold over the anterior wall of the stomach. We have frequently used the omental graft as a reinforcement. There is, however, adequate clinical and experimental evidence to warrant the use of the living omental graft, and this may be used if desired, or if there is great edema of the stomach wall. All studies show that the bacterial infection in the peritoneal cavity and its results are the major cause of death in perforated peptic ulcers. Microorganisms are to be found in the peritoneal cavity soon after perforation because, as has been said before, the gastric acidity is low and bacteria are found in gastric contents. The peritoneal fluid obtained at operation has a hydrogen ion and a chlorine ion concentration approaching that of blood plasma and, therefore, would not be in itself conducive to severe chemical irritation.

Gastrectomy has been advised in the treatment of acute perforation. We have not found this necessary nor do we consider so extensive a procedure to be indicated. In those who have recurrent ulcer as determined by symptoms, signs, and fluoroscopic examination by barium meal, radical operation can be done at a second time or a second stage. The percentage of patients requiring secondary operation is between 10 to 15 per cent.

Obstruction.—Obstruction of the stomach requires surgery. However, this should not be attempted before emptying the stomach and keeping it empty for at least a week to ten days. It is a well-known fact that the dilated stomach wall has poor healing qualities. First, the blood supply is reduced to the stomach wall; second, the musculature and the mucosa and serosa have been stretched so that they are not in a normal state of tone. Therefore, the Levine tube is introduced and suction applied and the

more, it is important to know that the polypoid variety of gastric carcinoma portant in the treatment, for in the sessile variety it is perhaps wise to include a portion of the stomach wall, whereas in the polypoid variety the mucosa must be excised, but not necessarily the outer layers of the stomach wall.

Malignant Tumors of the Stomach

Malignant tumors of the stomach may be divided into epithelial and connective tissue types. The epithelial types are the carcinomas which are the same variety of carcinomas found elsewhere in the body. Chief among varieties of carcinoma are the adenocarcinoma, medullary, scirrhous, mucoid type, and the ulcerating type. The sarcomas include lymphosarcoma, fibrosarcoma, myosarcoma, angiosarcoma, and malignant endothelioma. By far the most common malignant lesion of the stomach is carcinoma.

Carcinoma of the Stomach

The stomach is probably the most frequent site for carcinoma, with the female genital tract and breast second. Carcinoma of the stomach is most common in men. It is said to cause more deaths than cancer of the lip, tongue, cheek, tonsil, pharynx, larynx, salivary glands, thyroid glands, male and female breast, ovary, uterine cervix, and corpus uteri combined, according to Livingston and Pack. According to Wangensteen, it ranked next to cardiac disease in this country, and of the 150.000 annual deaths from cancer in the United States, approximately 40,000 persons die of gastric cancer. The cause of the disease is unknown. Many theories exist as to the probable cause, and most of these concepts have been discussed in Chapter 15.

Clinically, there does seem to be a very close relationship between carcinoma of the stomach and pernicious anemia. One cannot say which is the cause and which is the effect, but this much is known: in a study of autopsies on individuals 45 years of age or over, 293 cases of pernicious anemia were found. Thirty-six of the latter also presented carcinoma of the stomach, an incidence of 12.3 per cent, which is more than three times as great as the incidence in the remaining autopsies of the individuals of the same age (Kaplan and Rigler). Other relationships which have been advanced to explain this disease are the transforming of a benign polyp or a gastric ulcer into a malignant growth and, last, the theory that atrophic gastritis plays a role. This idea, of course, gains its strong support from the work just cited, showing the frequency with which pernicious anemia is complicated by gastric cancer. Many other theories have been invoked such as the age incidence, which is usually said to be over 45. In our experience, this has not necessarily been true, because a fairly large group of patients under this age have been discovered with cancer of the stomach. The incidence in women is not as low as formerly thought. The hereditary nature or familial tendency toward cancer of the stomach is no greater than the tendency toward the disease in other

gastric growths. Depending upon the type, various possibilities as to their pathological trends are inherent. They may be complicated by bleeding or ulceration or, if they are extremely large, by obstruction. If small, they may find their way beyond the pylorus, acting as an intermittent obstructive lesion. This is particularly true of polyps. Another interesting complication of polyps is the high instance of achlorhydria. This makes the diagnosis of pernicious anemia, carcinoma, and benign growths a very difficult one to make. The symptoms and signs may vary from nothing except an occasional complaint of indigestion to those resembling advanced carcinoma or chronic peptic ulcer. Many individuals are diagnosed as having pernicious anemia and treated on that basis for periods of time until the true nature of the stomach lesion is discovered by x-ray examination.

The *diagnosis* is made by careful physical examination, gastroscopic examination, and fluoroscopic observation with the barium meal. If a polyp is discovered and the symptoms and signs of pernicious anemia are present, the possibility of malignancy degeneration must be borne in mind. The authenticity of the diagnosis of pernicious anemia has been established in these cases by blood smears, bone marrow studies, the presence of glossitis, the findings of subacute combined sclerosis, and achlorhydria after histamine, and the clinical and hematological response to liver therapy. The benign polyp may undergo a rapid change into malignancy, and to confuse the picture still more, very often benign and malignant tumors may exist side by side. Large benign tumors may give no symptoms at all until malignancy has been discovered. Metamorphosis from a small barely detectable lesion to a large inoperable carcinoma has occurred within a period of months in the experience of many observers. Patients with pernicious anemia should have a semiannual x-ray examination of the stomach. Although this will not discover all carcinomas or benign tumors of the stomach, yet in a large percentage these will be discovered at the earliest possible time. About 5 to 10 per cent of the patients who develop cancer of the stomach will have a pernicious anemia. *Treatment* of benign tumors is surgical removal. When discovered at operation or diagnosed preoperatively, these growths should be examined by opening the stomach. They should be removed, including the base, which may then be cauterized. Frozen sections should be made and then if there is any doubt, gastrectomy should be done. If none, and if the growth is benign, the local excision may be sufficient. In a large series of studies, as has been mentioned previously in this chapter, there are approximately 10 per cent of normal persons who have achlorhydria; about 5 per cent remain achlorhydric after two doses of histamine. It is significant that in this group may be found a fairly large percentage of patients with benign polyps. Furthermore, iti s important to know that the polypoid variety of gastric carcinoma is not very common, although this type is the most favorable for complete extirpation. Therefore, the sessile growth of epithelial variety is much

The Symptoms and Signs of Carcinoma.—Unfortunately the disease presents so many symptoms and signs and they are so variable that no group is pathognomonic. In fact, many patients have no symptoms at all, until the growth is beyond control. The older textbooks of surgery always included the presence of a mass. In our experience, when this is felt, surgery is palliative at best. The most consistent symptom is that which might be termed as persistent or recurrent indigestion. When this is found in a man past 40 years, x-ray examination with the fluoroscopic study of the barium meal should be done. If nothing is found and the symptoms persist, x-ray should be repeated at six-month intervals. Another important aid is the study of repeated blood counts, because this is a very important guide to possibilities of the growth. In addition to the fluoroscopic examination, the blood count, and careful study of symptoms and signs, the gastroscope may be of value. However, in many instances, in our experience, this too has failed, because often the lesion is difficult to find with the scope or is beyond the reach of the scope.

The problem of discovering the disease is intimately related to the rapidity with which it grows. If it is slow growing, no symptoms will be manifest, and if it is rapidly growing, symptoms will occur in direct

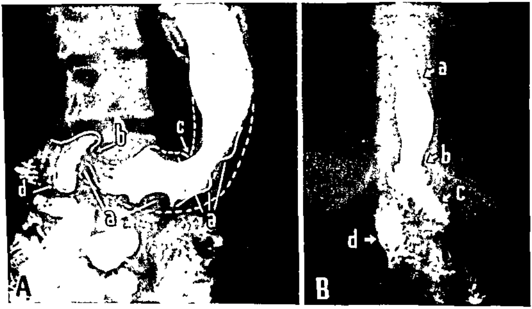


Fig. 286.—Linitis plastica or diffuse infiltrative colloid carcinoma accompanied by extensive fibrosis. *A*. Preoperative x-ray film. *a*, Filling defects; *b*, pylorus, *c*, incisura, *d*, duodenal bulb.

B. P., a woman 47 years of age, complained of loss of appetite, pain in the epigastrium while eating, and heaviness in the epigastrium. The patient had lost approximately twenty-five pounds in less than six months. X-ray examination of the gastrointestinal tract showed a "J" type stomach with defects in both the lesser and greater curvatures. At operation the entire stomach was involved by a diffuse carcinomatous process and accordingly a total gastrectomy was done. The jejunum was brought up to the esophagus as illustrated in Fig. 282. *B*. X-ray photograph showing the condition of the patient four weeks after surgery. *a*, Esophagus; *b*, site of anastomosis; *c*, proximal jejunal loop; *d*, distal jejunal loop. This patient recovered, lived for about two years, and then died of recurrence of the carcinoma. The type of operation performed is illustrated in Fig. 282. (Berman, J. K., and Fant, J. R.: Complete Resection of the Stomach; Quart. Bull. Indiana Univ. M. Center 3: 109, 1941).

parts of the body. Here, again, carcinoma behaves as an organ disease rather than a system disease, although exceptions to this statement are not too uncommon.

Pathological Studies.—Carcinoma of the stomach may take any of the different forms of carcinoma listed in Chapter 15. The more common varieties are the adenocarcinoma or the medullary type, which gives rise to a fairly large ulcerative growth, and the scirrhous carcinomas, formerly called "leather bottle" stomach. In between these groups are various subdivisions. Not infrequently the growth grows centrifugally, and in such cases negative x-ray findings are the rule. However, by the same token, since the growth grows externally, there is early metastases to regional nodes and adjacent organs. We have seen carcinoma of the

Fig. 285.—Adenocarcinoma of the stomach in a man aged 52 years. Arrow points to a probe which has been introduced in a perforation which caused the death of the patient.

greater curvature involve the greater omentum and transverse mesocolon as well as the transverse colon and still have a normal fluoroscopic examination with the barium meal. The scirrhous variety has also been called "linitis plastica" and was formerly thought to be due to syphilis. This has been disproved. Other varieties of carcinoma are carcinoma simplex and mucoid carcinoma.

Some times carcinoma of the stomach will grow very rapidly and cause symptoms of obstruction by its size. Sometimes it will perforate, although this is not common. Rarely multicentric carcinoma of the stomach may occur. In the upper portion of the stomach, extension of the growth may involve the esophagus. However, the phenomenal observation by all men who are familiar with the disease is that it rarely extends into the duodenum, although carcinoma of the duodenum does occur, both as a primary and secondary entity.

period without recurrence, the outlook for cure is extremely good. Another surprising observation made by many surgeons has been the fact that even in the presence of metastasis, palliative resection may prolong life so that the patient lives in comparative comfort for up to three years. This includes a small group in which resections were made in the presence of involvement of the liver, and the metastatic nodule has been removed from the liver. The best results are, of course, in those patients who have a small limited type of lesion. However, in the more extensive varieties radical surgery, including removal of all organs or tissues involved, may occasionally produce a cure and should be tried.

Treatment.—The treatment of carcinoma of the stomach is radical, complete surgical extirpation including the lymphatic extensions wherever

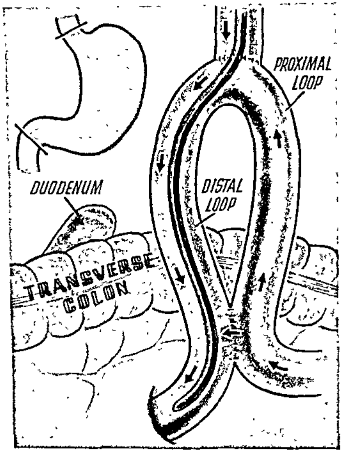


FIG. 287.—Diagram of operation done on patient reported in Fig. 286. Total gastrectomy with an anastomosis of the esophagus to the jejunum is done in cases of extensive carcinoma. The diagram illustrates the anterior method with jejunojejunostomy. This is done so that the pancreatic juice and bile may find its way across into the distal loop without having to go up into the esophagus and then down again. In producing the jejunojejunostomy, the anastomosis may be low down as illustrated in the diagram, or high, in which case if long enough it may simulate an artificial stomach. There have been various modifications of this procedure. For example, the jejunum may be brought up posterior to the transverse colon, or the duodenum may be brought up to the esophagus with an end-to-end anastomosis. Also, the jejunum may be divided, brought up to the esophagus and sutured as an end-to-end anastomosis and then its proximal end anchored to the side of the jejunum in the manner of a Roux Y anastomosis. The diagram gives the false impression that the distal loop penetrates the transverse mesocolon.

proportion to the rapidity with which it distends the organ. However, since the stomach has a large capacity, even this will be late. Blood in the stool may give a lead, but it takes over 7 c.c. of blood to be detected grossly, and the chemical test for blood must be carefully controlled since bleeding anywhere along the gastrointestinal tract will give a positive result. In an effort to discover the disease in an earlier state, mass fluoroscopy was done and, according to Harvey, after fluoroscopic examination of 2,413 men and women, only three cases of gastric carcinoma were found. Daily and Miller examined 500 apparently healthy men over 45 years of age, and no cases of proved gastric carcinoma were discovered. Since the discovery rate is so small, it is hardly worth while to use this as a method of attempting to find the disease in the early stages. Unquestionably in all of the studies, a large percentage of the patients examined will prove to have carcinoma later, but fluoroscopy is not the method by which the disease may be discovered in its early phases. Therefore, we may reiterate that a persistent or recurring indigestion of any sort in a man past 40 years should be carefully watched by repeated x-ray examination.

In the late stage a mass may be felt, and there is considerable amount of pain. Usually when this state is reached, nothing but a palliative operation can be done. Certainly a cure would be rare. In the late stages there is severe pain, but in the early stages the disease is notorious for its lack of pain.

The diagnosis is confirmed only by surgery. However, when the x-ray shows an organic lesion in the stomach, whether it be interpreted as a benign ulcer or other type of lesion, in our opinion, exploration is indicated. Even with the lesion in the surgeon's hands, diagnosis is often times impossible by gross examination and can only be made after microscopic study from the biopsy of the tissue.

The *prognosis* in carcinoma of the stomach is poor. Even with the most radical types of surgery, the percentage of five-year cures is extremely small. Various groups of statistics do not agree with the foregoing statements. One group of figures shows that the five-year survival rate of those who come through the operation is approximately 25 per cent; ten-year survival, 20 per cent; fifteen-year survival, 15 per cent. Of patients who did not have an extension or metastasis, 44.7 per cent are said to have lived five years after leaving the hospital. In contrast to these optimistic figures are those of another group of investigators who aver that five-year survival of unselected patients with gastric cancer is probably in the range of 2 per cent. In our experience the five-year survival rate is approximately 4 per cent. We use the term survival rate rather than cure because the percentage of those definitely cured is probably lower than this figure, but we may say that 5 per cent are alive and symptom free at the end of five years. If no operation is done, none are alive at the end of three years. For those who survive the five-year

a small group has shown that most of the patients live only from one and one-half to two years after total gastrectomy. The operation of partial gastrectomy has been described under the discussion of peptic ulcer. Total gastrectomy implies the removal of the entire stomach, including a cuff of duodenum as well as a cuff of esophagus. In this operation, done through a thoracoabdominal incision, if necessary the spleen, pancreas, and transverse colon also are removed, and any other organs which have been involved may be extirpated in part if necessary. Then the jejunum is anastomosed with the esophagus and an entero-enterostomy is made between the two loops of the jejunum. It has been our custom to make this anticolic. However, many prefer to bring the jejunum up through an aperture made through the transverse mesocolon.

Complications of *total gastrectomy* include diarrhea, dysphagia, and biliary regurgitation. The loss of the intrinsic factor of Castle should cause an anemia, but in our experience it does not do so. A mild secondary anemia is present as in any gastrectomy operation, but this may be easily controlled with liver and iron therapy. It has been our custom to take out the Levine tube after anastomosis has been done; also an enterostomy has been made for feeding in many instances, particularly in patients who are badly debilitated and in whom adequate preparation was not feasible prior to surgery. The tube is left in the stomach after vagotomy and after esophagectomy because the stomach becomes inactive. The presence of a foreign body after an anastomosis is certainly to be looked upon with a great deal of concern because it stimulates secretion and may increase the exudative phase and thereby prolong healing.

Carcinoma of the Duodenum

Primary carcinoma of the duodenum is a very rare condition; its incidence is reported as from .03 to 0.003 per cent of all autopsies. In other words, the percentage varies from 3 in 10,000 to 3 in 100,000 autopsies. Carcinoma of the ampulla of Vater is a more common lesion and is seen more frequently. This lesion is easier to diagnose because of the early obstruction to the common bile duct and, therefore, the possibility of the disease is entertained. However, in primary carcinoma of the duodenum, the lesion can be detected only by x-ray examination or the presence of obstruction due to its size. The treatment of carcinoma of the duodenum, exclusive of the ampulla of Vater, consists of resection of the duodenum or the portion of the bowel involved together with restoration of gastrointestinal anastomosis. In carcinoma of the ampulla of Vater, however, this may also demand resection of the duodenum which is so intimately related to the pancreas that pancreaticoduodenectomy may be necessary; in other words, the Whipple operation. At any rate, the growth should be excised in its entirety, and in carcinoma of the ampulla of Vater, the head of the pancreas may have to be removed in part, if not in its

they may occur. In several instances it has included resection of the transverse colon together with a radical resection of the stomach. Sometimes the head of the pancreas may be resected if it is involved. Again lymph nodes which are in juxtaposition to the common bile duct must be removed if the entire disease is to be eradicated. Total gastrectomy is sometimes necessary when the lesion involves so much of the stomach that leaving part of it would be hazardous. The mortality for total gastrectomy is about 15 to 20 per cent. However, some statistics quote a mortality rate of as low as 10 per cent. Obviously this will vary with the type of patient committed to surgery and the extensiveness of the disease. Certainly it is a justifiable procedure and should be done wherever the condition of the patient makes it at all feasible.

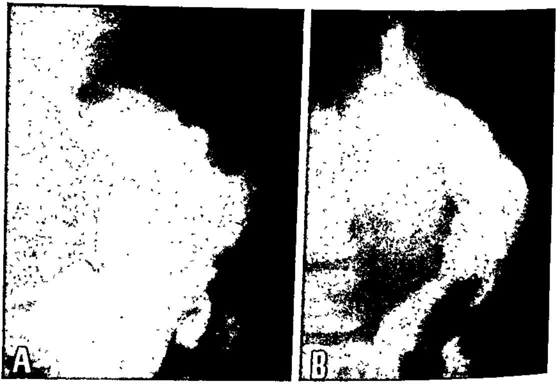


Fig 288.—Carcinoma of the upper third of the stomach in a man, 52 years of age, whose chief symptoms were those of pain, occasional vomiting, and loss of weight. *A*. X-ray photograph showing the preoperative condition. Note the irregularity of the upper third of the stomach and the lower end of the esophagus. At operation a very large adenocarcinoma was encountered involving the entire upper third of the stomach and the lower portion of the esophagus. It had invaded the gastrocolic omentum to a small degree and had spread to the pancreas and the gastrosplenic ligament. A total gastrectomy, splenectomy and resection of the tail of the pancreas was accomplished and then the jejunum was brought up to the lower third of the esophagus as shown in the postoperative x-ray photograph *B*. The surgical approach was a combined thoracoabdominal incision. The exposure by this incision was excellent, and the lower third of the esophagus could be easily resected along with the entire stomach, tail of the pancreas, spleen, and a portion of the gastrocolic ligament. The patient, at the end of one year, was without apparent recurrence.

The recurrence rate after a total gastrectomy is not so encouraging because it is very high. In our experience it is even higher than after partial gastrectomy. This is to be expected because the extent of the disease made the more extensive operation necessary. Our experience with

causes may be included such as prolapse of a benign tumor through the pylorus, transpyloric prolapse of the mucosa, intussusception, volvulus. Most of these conditions have been described previously in this chapter. However, we have not considered the effects of prolapse of the mucous membrane, intussusception, and volvulus.

Prolapse is a rare condition and is so intimately connected with the pedunculated adenoma or polyp that the two conditions are difficult to differentiate. Usually there is an associated pyloric stenosis. The diagnosis is made by the symptoms and signs of obstruction and careful fluoroscopic study with barium meal. The treatment for the condition is to remove the benign tumor, if this is the cause, together with its pedicle, as has been previously described. In cases in which there is a prolapse of the mucous membrane, the treatment of prolapse consists of making a longitudinal incision through the pylorus, excising the redundant mucous membrane and closing the pylorus in a transverse manner in accordance with the Heineke-Mikulicz pyloroplasty.

Intussusceptions occur all along the gastrointestinal tract. The most common site is the terminal ileum and consists of an ileocecal intussusception. This will be described later in the chapter. Rarely an intussusception of the stomach will occur along with a submucous fibroma of the stomach or other types of benign tumors, very much like an intussusception caused by a Meckel's diverticulum in the ileum. Here, again, the diagnosis is difficult to make except that the symptoms and signs lead to the supposition of a stenosis or an obstruction, and the diagnosis is confirmed more or less adequately by the barium meal and fluoroscopic examination. Treatment of the condition is surgical and includes the reduction of the intussusception in a retrograde manner. If this cannot be done with ease, a pyloroplasty may be necessary to accomplish it. In addition, the removal of the benign tumor, if this has been the cause, is indicated.

Gastric volvulus has been reported infrequently. It consists of a torsion from left to right or from right to left and rotation upward. The torsion must be a 180 degrees or more in order to produce an obstruction. The cause of the condition is usually a very redundant gastrohepatic ligament. It must be remembered that the stomach originally is a straight tube and that its lesser curvature faces anteriorly. Failure to rotate may produce partial torsion or volvulus, but these cases rarely produce symptoms However, they leave the patient with a long gastrohepatic ligament so that a torsion may occur. The diagnosis is made by symptoms and signs of obstruction which are usually extremely high and are thought to be in the cardiac orifice. X-ray is not of great value because the barium may not find its way into the stomach. Exploratory operation is usually done to determine the cause, and this is readily observed at the time of operation. Volvulus is reduced and several tucks are made in the gastrohepatic ligament to prevent the recurrence of the abnormality.

entirety, at the same time. The common bile duct is then transplanted into the jejunum, and the latter is anastomosed to the divided stomach as is done in a partial gastrectomy, as previously described. This operation, which has come to be known as the Whipple operation, will be described again under the discussion on carcinoma of the pancreas in Chapter 22.

Sarcoma of the Stomach

Sarcoma of the stomach occurs in the form of a leiomyosarcoma which is rare or a lymphosarcoma or any of the other combinations of tissues with which it may be involved. Leiomyosarcoma is interesting because it has been thought that this lesion may be the cause of the pernicious anemia rather than the reverse. (See discussion on Carcinoma of the Stomach.) In many cases of pernicious anemia there is a hypertrophy of the pyloric musculature, which, after all is what leiomyosarcoma consists of except that it has neoplastic components. Lymphosarcoma is a lesion of the stomach with very rapid potentialities and growth. Because of this rapidity of growth and because of the great variability in age with a tendency toward the more youthful patients, lymphosarcoma may be suspected preoperatively. If the x-ray shows a large organic lesion, probably carcinoma, the disease may be suspected. Roentgenologists sometimes are able to make the diagnosis because of the smooth margins of filling defect and the localized infiltration which it usually shows. This is not at all pathognomonic and, therefore, it is at best a guess. Sometimes the therapeutic tests by x-ray treatment will make the diagnosis, because reticulum-cell sarcoma and the small round-cell sarcoma are sensitive to x-ray, particularly the latter type. Usually the lesion will be diagnosed as a carcinoma, and gastric resection will be made before the diagnosis can be established.

Sarcoma of the Duodenum

Sarcoma of the duodenum is extremely rare, and only a few cases have been reported. Here, too, the diagnosis is usually that of carcinoma of the duodenum, if that diagnosis can be made, and the nature of the lesion is discovered when microscopic examination or biopsy is made.

The treatment for the lesion is the same as that for carcinoma, although the response to x-ray therapy is encouraging. Usually response is transient and the lesion will recur if x-ray alone is used. Occasional cures have been reported.

Obstruction of the Stomach and Duodenum

Obstruction may be caused by congenital anomalies such as atresia or stenosis, by congenital hypertrophic pyloric stenosis which occurs in the first six weeks of life, inflammations such as corrosive gastritis, peptic ulcer, new growths including benign and malignant tumors, and foreign bodies such as the bezoars. In addition, a miscellaneous group of

The prevalence of this congenital abnormality warrants inspection of the terminal ileum for possible Meckel's diverticulum in abdominal explorations.

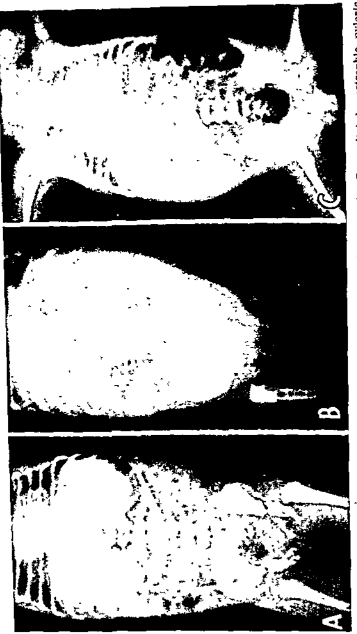


Fig. 289.—Types of congenital obstructions in the gastrointestinal tract. *A*. Congenital hypertrophic pyloric stenosis in an infant. A small amount of barium was given. Note the enormous dilatation of the stomach. Rammstedt pyloroplasty was successfully done. *B*. Congenital atresia of the ileum. Flat plate of the abdomen shows absence of gas in the colon and distention of small bowel and stomach above the obstruction. At operation a congenital atresia of the lower ileum was found. Double enterostomy was performed and then resection and lateral anastomosis done four days later. *C*. Imperforate anus in a newborn infant. X-ray made in the upside-down position, revealing the position of the blind hind-gut. Operation was done from below. The hindgut was brought down to the perineum, with good recovery.

The foregoing discussion shows that Meckel's diverticulum may have various pathological changes, the most common of which are inflammation leading to a diverticulutis, heterotopia of gastric mucous membrane, with peptic ulcer and hemorrhage, and intestinal obstruction with intussusception or volvulus. In the latter group it should be mentioned that we have recently seen an 18-month-old baby who had an acute Meckel's

THE MID-GUT

The mid-gut includes the small bowel from the duodenal papilla down to the middle of the transverse colon. It will be convenient to discuss the lesions of the small intestine as a group and then include the cecum with the rest of the colon in another group.

Congenital Anomalies

We have already discussed earlier in the chapter congenital anomalies of the small bowel. These include atresia, stenosis, malrotation, and duplication. We have also described enteric cysts which are probably another example of duplication. Duplications occur in the large intestine including the appendix. Indeed duplications of the entire large bowel have been reported and even a case of triplication of the large intestine is on record. The enterogenous cysts have been described under the term of enteric cysts, enterocystoma, ilium duplex, and unusually Meckel's diverticulum, giant diverticulum, etc. In our discussion of the peritoneum and mesentery we described congenital cysts, subdivided into lymphatic or lymphangiomatous cysts, urogenital cysts, dermoids or teratomas, developmental cysts, and inflammatory cysts due to intrauterine accident. In the latter group we also included a localized collection of pus which follows a perforated diverticulum or duplication which may be completely encapsulated and surrounded by connective tissue, producing an inflammatory cyst of nonspecific bacterial origin.

Meckel's Diverticulum.—It is generally believed that in 2 per cent of normal adults some remains of this diverticulum are present. The literature is full of various reports concerning changes which may occur in the diverticulum or as a result of its presence. Heterotopia of the mucous membrane and associated glands, superficial and deep, may occur and become implanted in various portions of the alimentary canal. The esophagus, stomach, pancreas, common bile duct, and lung all are part of the original endodermal canal and its derivatives in the 5 mm. embryo. This explains the possibility of heterotopia.

Greenblatt divides the various groups into the following divisions:

1. Peptic group in which gastric mucosa is present with ulcers, hemorrhage, or even perforation.
2. Obstructive group which may give rise to intussusception, volvulus, bands and adhesions, contents of inguinal or femoral hernia.
3. Diverticulitis group which may be simple acute, acute with perforations, and gangrenous or chronic.
4. Umbilical group which may give rise to fecal fistula, umbilical adenoma, or prolapse of intestine through umbilical fistula.
5. The tumor group which may be benign, malignant, or heterotopic tissue such as pancreatic tissue or embryonal rests.
6. Incidental group which contain normal intestinal structure.

Heterotopic gastric mucous membrane may produce a definite syndrome in adults. It probably represents an ulcerative condition in the diverticulum and the marginal portion of it. Rarely, Meckel's diverticulum may be the seat of carcinoma. Approximately nine cases have been reported which were adenocarcinomas of the intestinal mucosa. We have seen one case of adenocarcinoma of gastric mucosa in a child of 7 years.

The diagnosis of a Meckel's diverticulum which is not the seat of a pathological change is extremely hard and cannot be made even with the aid of x-ray, although occasionally the roentgenologist may be able to demonstrate it by giving a barium meal and following through with films every half hour. The inflammatory lesions are frequently mistaken for appendicitis, and it is our custom to examine the last two feet of ileum in all cases of diagnosed appendicitis in which the appendix is found to be normal. Not infrequently the surgeon is rewarded by finding an inflamed diverticulum. The heterotopic mucous membrane of gastric origin in the diverticulum leads to an ulcer which in turn may cause perforation or hemorrhage; usually the chief symptom is hemorrhage which, in a child, is bright red, and it may be profuse. It invariably leads to the suspicion of a Meckel's diverticulum.

Hemorrhage in the child requires careful consideration of the following possibilities: (1) Meckel's diverticulum with peptic ulcer. (2) Intussusception. The symptoms and signs will be discussed later. (3) Duplications of the terminal ileum in which there is a connection between the pouch of the ileum with the lumen of the normal bowel. Ulceration occurs and hemorrhage takes place. (4) A single polyp in the lower colon which may sometimes produce severe bleeding in the child. (5) Multiple polyposis which also occasionally produces bleeding. Although multiple polyposis produces bleeding invariably, hemorrhage is not as common as from a single large polyp. We have seen several cases in which the polyp is in the small intestine rather than in the large bowel. The diagnosis of polyposis is by x-ray or proctoscopic examination. Some of the rare causes for bleeding in the child are: (1) duodenal ulcer; (2) hemangioma of the intestine; (3) Banti's syndrome with portal hypertension; (4) a hypertrophy of the lymphoid tissue of the ileum which may occasionally be seen in the child with ulceration and bleeding; (5) very rarely, terminal or regional ileitis which has been reported in the child with bleeding; (6) extremely rarely a jejunal diverticulum with ulceration—occasionally there may be multiple diverticula of the small bowel. (7) Two cases of repeated massive hemorrhage and the passage of bright red blood by rectum have been reported due to neurofibroma of the ileum. This is extremely rare.

Intestinal Obstruction

Anything which interferes with the propulsion of the contents of the intestinal tract causes marked local symptoms throughout the entire

diverticulitis, and the child was admitted to our service at the Methodist Hospital. The diverticulum was attached to another loop of small bowel, and then the proximal portion of the ileum rotated itself around this newly created band, formed by the diverticulum and its adhesions, to an adjacent loop of small intestine, producing a volvulus with gangrene. Resection was necessary with lateral anastomosis. This was done in two stages, but the *second stage was done within eight days after the first stage.* The reason for this is that children of this age group withstand enterostomy poorly, and the mistake that has been made in the past has been

Fig. 290.—Meckel's diverticulum with intestinal obstruction. *X-ray photograph* of a scout film of the abdomen in a 2-year-old child who came to the hospital complaining of persistent vomiting, no bowel movement, enormous distention, fever of 106° F. and extreme abdominal tenderness. The diagnosis was that of obstruction in the lower ileum with perforation and peritonitis. The child's blood count was 23,000 leucocytes with 95 per cent polymorphonuclears. A Levin tube was anchored, suction applied, and water balance restored. At operation an intussusception was *encountered* due to a Meckel's diverticulum with gangrene of the intussusceptum. Due to the precarious condition of the child, the intussusception was resected and the two ends of the ileum brought out through the incision in the manner of a double-barrel enterostomy. Four days later the child was operated upon again and the enterostomy was taken down, both ends inverted, and a side-to-side anastomosis done. The child was last seen in April, 1949. At this time he was in perfect health. (Case *referred by Dr.* S. Kaufman.)

that the child was permitted to have the enterostomy as long as an adult, which is wrong because water balance cannot be maintained. By doing the second stage eight days after the first, the child's condition was improved sufficiently so that a successful anastomosis was established. The child made an uneventful recovery.

tinal obstruction these three factors must be considered. *Mechanical obstruction* is produced by some organic cause which occludes the bowel from within (obturation), or within the bowel wall itself, or from without (compression). *Obturation* is caused by congenital anomalies (atresia, stenosis), new growths such as carcinoma of the pylorus and carcinoma of the colon or rectum, large polyp, foreign bodies such as barium meal, fecal impaction, a large gallstone which has eroded through the gall bladder into the bowel, or the rare bezoars, balls of hair (trichobezoar) or plant fiber (phytobezoar). Within the bowel wall may be listed inflammation (regional enteritis), trauma, thrombosis, hemorrhage, embolism, and strictures from regional enteritis or colitis, lymphopathia venereum, syphilis, and tuberculosis, diverticulitis, intussusception. *Compression* is caused most commonly by postoperative dense adhesions or bands. A more transient variety occurs after perforative appendicitis, or diverticulitis, due to inflammatory swelling. Incarcerated, or strangulated, hernia is also a very common cause, and, in addition obstruction may be caused by internal hernia, due to congenital bands or defects in the mesentery, especially in the mid-gut and diaphragmatic hernia. External tumor masses, abscesses, or inflammatory masses may compress the bowel. In children, obstruction may be due to *intussusception* (or telescoping) of the bowel, caused by small tumors (polypi) in the lumen, or congenital defects in the wall or in its nervous innervation. It usually occurs at the ileocecal valve, and because it does not produce complete obstruction until late, it is apt to present difficulties in diagnosis. In infants, congenital anomalies such as Meckel's diverticulum (complicated), malrotations, and bands may cause obstruction. *Volvulus* is a twisting of the bowel on its long axis. It is more common in the aged, but may occur in the newborn. There is always a long mobile mesentery.

There is another cause of obstruction due to an imbalance of the autonomic nervous control of the bowel. *Overaction* of the sympathetic and parasympathetic nerves supplying the muscular coat causes intense and prolonged spasm known as *dynamic* or *spastic ileus.* Or there may be an impairment of motor function, leading to inhibition, *adynamic* or *paralytic ileus.* This is an improper term because the bowel is not completely paralyzed as evidenced by the passage of the Miller-Abbott tube. The former is seen in angioneurotic edema, lead colic, or toxic food poisonings. The latter is most commonly seen in inflammatory lesions of the peritoneal cavity with *peritonitis.* However, reflex causes, from disease or injury outside the bowel or even outside the peritoneal cavity, may cause a paralytic ileus. Some of the more commonly encountered causes are postoperative ileus (due to prolonged handling of the intestines), biliary and renal colic, twisted ovarian cyst, pneumonia, spinal or hip fractures, tabes dorsalis, and injuries to the spinal cord. Mesenteric thrombosis or embolism and pancreatitis may also cause a paralytic ileus. The former is distinguished from the latter by the presence of blood in

alimentary canal and also affects the patient as a whole, not infrequently causing death. This interference may be acute or sudden in its onset, though the actual cause may have been present for some time. It may be chronic, due to a stricture or band, and in this case it must necessarily be an incomplete obstruction. If the loop of bowel is occluded sufficiently to obstruct the fecal current without damaging the blood supply, it is known as *simple obstruction*, whereas if the blood supply is impaired, it is a *strangulated obstruction* and leads to gangrene of the bowel. Obstruction of the upper bowel, or *high* obstruction, occurs in the pylorus, duodenum, jejunum, and upper ileum, whereas the *low* variety occurs in the lower ileum or in the large bowel. The time element is important and physicians speak rather arbitrarily of *early* and *late* obstructions according to the severity of the symptoms as well as the duration of the obstruction.

Fig. 291.—Atresia of the ileum. Preoperative x-ray photograph of an infant, 24 hours old, who had vomited constantly since birth and whose abdomen was enormously distended. There had been no passage of flatus or meconium. The x-ray photograph reveals enormously distended loops of bowel which end in the right lower quadrant. At operation three distinct atresias were encountered. The first approximately 20 cm. from the ileocecal valve; the second, about 10 cm.; and the third at the ileocecal juncture. The entire lower ileum and cecum were resected and a side-to-side anastomosis was done. Between the areas of atresia the bowel was normal. The child had mild diarrhea for approximately six months following surgery. This probably occurred because of a *decrease in the absorption area of the large bowel.* However, when last seen in June, 1949, at 2 years of age, she was in excellent health. (Case referred by Dr. George L. Compton and Dr. H. Call.)

More important to the surgeon is the cause of obstruction. This occurs in one or more of three ways: (1) Occlusion of the intestinal lumen so that there is an actual barrier against the propulsion of enteric content; (2) lack of propulsive power due to decreased intestinal peristalsis; (3) embarrassment of the circulation which affects the movement of the bowel and decreases the size of the lumen by swelling. In every intes-

and coronary vasoconstriction which is produced not only by the vasovagal reflex but the anoxemia as well and results in more anoxemia due to cardiac inadequacy and stagnant anoxemia. Here oxygen, as well as atropine, in deeded.

The sludge in an obstructed loop is toxic. It is composed chiefly of dead bacteria. The supernatant fluid is nontoxic. Normal intestinal content is more toxic than the material from an obstructed loop when injected intravenously into experimental animals. There is experimental evidence to show that in an obstructed loop outside the abdomen, absorption will not take place unless the pressure in the loop is less than diastolic. In the abdomen there is absorption, even if the distended loop has a pressure above systolic, due to diffusion through the bowel wall. This absorption is limited by adhesions. The chief dangers are perforation and peritonitis. Strangulation usually occurs from *outside* interference with the blood supply. However, *inside* pressure may be so great as to cause gangrene. This occurs usually in the duodenum or ileum, rarely in the stomach or large bowel, due to the fact that the blood vessels enter the wall of the duodenum and ileum at the mesentery, whereas in the stomach and colon, they almost surround the wall before they enter it. In all types of obstruction, local thromboses ultimately occur. Some absorption occurs through marginal veins in loops that are greatly distended with gas. The intestine of the dog is very muscular and he vomits easily. The rabbit cannot vomit and therefore death occurs early from gangrene and perforation.

Symptoms, Prognosis, and Treatment of Intestinal Obstruction.—The cardinal *symptoms* and *signs* are persistent vomiting, which becomes steadily more stercoraceous, violent cramplike pain, absolute constipation, including an inability to expel flatus, distention, and absence of bowel sounds. *Early*, the vomiting is not fecal in character, cramps are slight, and sounds are present and strong, due to violent peristalsis, and there are slight distention, constipation, and few constitutional symptoms (simple obstruction). *Later*, the vomiting becomes dark and foul, bowel sounds are not heard, distention is great, and constitutional symptoms are prominent (obstruction with strangulation). The greatest help in diagnosis is derived from a scout x-ray plate of the abdomen. It will show the typical stepladder gas pattern and may indicate the site of the obstruction. Although the typical gas pattern may not be present, if there is gas in the small bowel of an adult, it means some type of obstruction. This is not true of children. Gas appears within a few hours after obstruction. Gas in the large bowel unless inordinate is normal. If in small and large bowel, an ileus is probably present. A barium enema is also helpful, but a barium meal should never be given. In addition, blood counts (showing hemoconcentration, high leucocytosis), blood chemistry (showing increases in nonprotein nitrogen and carbon dioxide combining power), and urinalysis (showing a high specific gravity and alkalinity) help to establish the degree of constitutional effects. There may be variations in these symptoms which are confusing to the novice

the stool. Also, in thrombosis, before complete occlusion of the vessel, there is pain following a meal. This is due to inadequate blood supply to the intestinal muscle—very much as in intermittent claudication in peripheral vascular disease.

Pathological Physiology of Intestinal Obstruction.—In simple obstruction the intestine attempts to force its content onward by strong and vigorous peristaltic waves. Since this is unsuccessful, the bowel *above* the site of obstruction is distended with gas and feces, and *below* the site of obstruction it is collapsed. Some reverse peristalsis occurs and vomiting is the result. This causes *dehydration* due to loss of fluid from the bowel (6 to 8 liters per day may be lost). Furthermore, loss of hydrochloric acid depletes the blood chlorides and causes a hypochloremia (except in pyloric obstruction due to carcinoma associated with anacidity). Since chloride exists principally as NaCl in the blood, sodium is retained, combining with plasma bicarbonate and causing an increase in sodium bicarbonate. *Alkalosis* results and the blood shows an increase in the carbon dioxide combining power. We have learned in Chapter 11 that the retention of body water is dependent upon electrolytes. In alkalosis there is a loss of base in the urine (chiefly sodium), which is accompanied by a loss of water, and there is a further loss of water into the obstructed loop, resulting in further dehydration. Absorption of food or water from the bowel does not occur due to disturbance in osmosis. In addition, there will be hemoconcentration and a rise in nonprotein nitrogen and urea (due to tissue destruction and renal impairment). If the bowel wall is damaged because of an impaired blood supply (strangulation), the selective absorptive power of the mucous membrane is lost. (Normally the mucous membrane selects for absorption substances useful to the organism.) When this occurs, there is *toxemia*, due to the absorption of toxins. Since the veins are occluded, the toxins are absorbed by being forced into the peritoneal cavity through the injured bowel wall by the intraluminal pressure. There will be a loss of plasma into the wall of the bowel and peritoneal cavity caused by anoxic anoxemia due to the great distention and stagnant anoxemia caused by venous stasis in the abdomen, which is also due to distention; last, the distention ultimately produces a local tissue anoxemia with leaky capillaries and edema of the bowel wall; thus there is loss of water and electrolytes, alkalosis, hypoproteinemia, and hemoconcentration. The latter increases the stagnant anoxemia, further deflecting plasma proteins; this, in turn, favors edema in the entire body, including the bowel wall, adding an adynamic ileus to all types of obstruction which persist. Contributing to the anoxemia as a result of an overdistended stomach is the coronary vasoconstriction which occurs in older individuals probably through a vasovagal reflex. In the experimental animal this reflex can be produced by overdistention of the stomach, and it can be abolished by sectioning the vagi or using large doses of atropine. Thus another vicious circle may occur in intestinal obstruction: anoxic anoxemia due to the great distention pushing upward on the diaphragm

The prognosis depends almost entirely on the time element. Most obstructions may be handled successfully if seen early, or if there is not too extensive involvement of the bowel.

The *treatment* will depend on the type of obstruction and the general condition of the patient. In general, there must be a correction of the local and systemic pathological disturbances as indicated and then a restoration of bowel function by surgical intervention. In all cases, lost fluid electrolytes and plasma must be replaced (see Chapters 11 and 14). Morphine is given to relieve pain and increase the tone of the intestinal wall. Decompression of the bowel with the Miller-Abbott or Levine or Harris mercury weighted tube and suction apparatus may sometimes cause an obstructed loop of bowel to be released without operative intervention. The Miller-Abbott tube is useful to deflate the bowel in mechanical as well as "adynamic" ileus. Deflation permits absorption of fluid and liquid food in the small intestine. After the tube has descended to the site of obstruction, a very small amount of barium may be introduced, outlining the obstruction and even revealing its cause in some cases. If left in place, the surgeon can immediately find the obstruction by finding the tip of the tube. It should not be left in too long because of injury to the larynx and ulceration of the aryepiglottic folds; also in devitalized bowel it may cause a perforation, and rarely esophageal varices are made to bleed by its use. We may conclude that the medical treatment of bowel obstruction is in every sense an emergency.

Surgical intervention is indicated for the release of the impinged or occluded intestine. Immediate operation should be done in all early cases or in those in which gangrene is suspected. The criteria for suspecting gangrene are (1) history of a sudden onset of crampy colicky pain coming in episodes with persistence of pain between the episodes, (2) palpable mass or localized tenderness, (3) fever, rapid pulse, and leucocytosis which persist in spite of treatment for dehydration. Sometimes it is difficult at operation to determine the viability of the bowel after it has been strangulated. Usually the application of warm moist packs will encourage the return of circulation if infarction with necrosis has not occurred. Other methods to determine viability include the fluorescein test. This consists of the intravenous injection of 5 c.c. of a 5 per cent solution of fluorescein, to which sodium bicarbonate has been added to make a 5 per cent solution. The rays of the ultraviolet bulb, which is covered with a purple glass filter, are directed on the questionable loop. Soon a golden-green color appears except in the areas devoid of blood supply. If, in addition, a 10 per cent solution of procaine is injected into the mesentery, the effects of vasoconstriction are diminished, permitting a more accurate evaluation of the blood supply. A quick and reliable test is the inhalation of 100 per cent oxygen which results in a prompt change in color in viable bowel. In late obstruction the operation may consist of enterostomy alone, or if gangrene is present, resection with enterostomy. Seldom will the

and mature alike. In *high obstruction* there are *early vomiting, no distention, early dehydration,* and *bowel movements* for some time, whereas in *low obstruction vomiting comes very late and distention is early* and there is no passage of flatus or stool. Paralytic ileus causes very little pain. In obstruction at the pylorus there is vomiting, but the vomitus contains no bile; in obstructions below the pylorus, the vomitus contains bile. In lower obstructions the vomitus is more stercoraceous than in those higher up in the intestinal canal. Obstructions of the small intestine and of the sigmoid are apt to be strangulated due to their long mesentery. In most obstructions of the large bowel (which *has no*

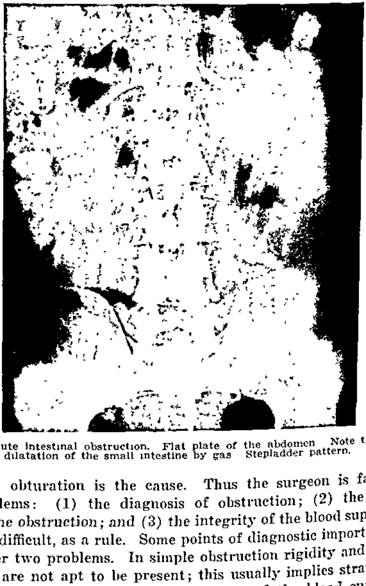


FIG. 292.—Acute intestinal obstruction. Flat plate of the abdomen. Note the enormous dilatation of the small intestine by gas. Stepladder pattern.

mesentery) obturation is the cause. Thus the surgeon is faced with three problems: (1) the diagnosis of obstruction; (2) the probable nature of the obstruction; and (3) the integrity of the blood supply. The first is not difficult, as a rule. Some points of diagnostic importance help in the latter two problems. In simple obstruction rigidity and localized tenderness are not apt to be present; this usually implies strangulation in small bowel obstruction with impairment of the blood supply. In simple obstruction gas may be centrally located with a transverse long axis, while in loop obstruction all sorts of bizarre patterns may be seen and proximal distention is slow.

two later. Early intestinal obstruction of any variety belongs in Group 1 and is probably best treated by surgery as soon as the patient can be properly prepared.

Group 2: An example of bowel obstruction which requires immediate operation, even though the patient's condition is unfavorable, is that of strangulation. The operation should be delayed only long enough to prepare the patient for surgical intervention. This is done by an attempt to replace the water-electrolyte loss and to replenish the loss of blood or plasma. The diagnosis of a strangulated loop is made when there is intestinal colic with vomiting, intestinal distention, and absolute constipation, combined with the signs of local inflammation and peritonitis. Usually the venous rather than the arterial circulation of the bowel is disturbed. Ultimately, however, the latter is also impaired when the pressure within the vein equals the arterial pressure. However, even before this stage, there is a tremendous passive congestion which soon gives way to hemorrhage in the tissues of the intestine, then into the lumen of the intestine, and finally into the free peritoneal cavity. This initiates the so-called "aseptic" peritonitis, although bacteria are probably present. The cardinal signs of peritonitis have already been described and include tenderness, distention, adynamic ileus, and a silent abdomen. Although there are local tenderness and rigidity over the area of strangulation, these may be absent when gangrene occurs. In addition, there are fever and leucocytosis, although these are found in all types of obstruction. If in doubt, the surgeon will prepare the patient and proceed with operation immediately in all cases of suspected strangulation. Here, again, the scout film of the abdomen will be of great help in distinguishing early strangulations from such conditions as perforated appendicitis or diverticulitis, because the film will show a distended loop of small bowel, whereas in diverticulitis or appendicitis there will be an ileus of the so-called paralytic type in which both large and small intestine may be distended. In volvulus, one large distended loop may be seen. Two conditions which may be indistinguishable by physical and roentgen signs from volvulus are mesenteric thrombosis and an internal strangulated hernia.

Another example of Group 2 obstruction is intussusception. This requires immediate operation in all instances to avoid gangrene. Reduction by barium enema is not advisable unless it should occur while the diagnosis is being made and even here it is not reliable.

Group 3: Examples of those conditions which are amenable to delayed operative intervention are the incomplete or intermittent obstruction. Careful studies should be made to reveal the site and nature of the obstruction so that a correct evaluation of the condition may be obtained. Such cases may be prepared by restoration of electrolytes, blood volume, and plasma, and the administration of penicillin and streptomycin; enemas may be tried to relieve discomfort. The causes responsible for this group of obstructions are gallstones or foreign bodies, internal hernia, loops of

surgeon elect to do a complete operation in late cases, because the patient's condition will *not* permit it. Later he may finish his work in a deliberate manner.

Some General Rules in the Treatment of Bowel Obstruction.—From the standpoint of treatment, intestinal obstruction may be divided into four groups based upon the pathology present and the condition of the patient: (1) Obstructions which require immediate operative intervention and in which surgery may be safely undertaken; (2) obstructions requiring immediate surgery in patients whose general condition may not tolerate it; (3) obstructions in which delayed operative intervention is feasible and desirable; and (4) those types of obstruction which may be amenable to nonsurgical treatment in patients not dangerously sick. Examples of the various groups may be cited.

Group 1: Complete obstruction of the transverse, descending, or sigmoid colon *must be considered as a closed loop obstruction* because of the competence of the ileocecal valve on the proximal side and the presence of the obstruction distally. Therefore, this type of obstruction when complete may cause tremendous distention and must be relieved by operative intervention. The Levin or the Miller-Abbott tube with suction will be useless because of the ileocecal valve. The diagnosis of this particular type of obstruction is *usually made by the history*. The patient will describe *successive attacks of cramping pains* with a change in the habit time of bowel action, finally resulting in more or less complete constipation. Also, he may tell of alternating diarrhea and constipation, nausea but rarely vomiting, and mucus and blood in the stool. The patient is usually 50 years old or over and he does not look ill. Physical examination shows early distention, however, bowel sounds may be *heard*. *Digital examination of the rectum will usually reveal the neoplasm.* If it is too high up for the finger to feel the mass, a proctoscopic examination may be done, and this will help make the diagnosis. If the physician depends upon the patient's history or statement that he can take a large enema and, therefore, cannot be completely obstructed, he will be misled. *It is true that the normal colon will accept a quart or more but usually not the obstructed one.* This is, however, a debatable type of criterion because many normal patients cannot accept much water by enema. Furthermore, it is not wise to introduce too much water for fear of perforation. X-ray studies *help* to confirm the diagnosis. A barium enema may be tried but *should not* be introduced under great pressure because *the barium will find its way above the obstruction where it becomes dehydrated and converts an incomplete obstruction into a complete one.* The barium finally becomes extremely hard and may be very difficult to remove before surgery. *A* scout film of the abdomen usually reveals the greatly distended *colon.* The type of operation in such cases will ordinarily be *palliative (that is, cecostomy or transverse colostomy)* and will be a preliminary measure to deflate and empty the colon so that this organ may be removed safely a week or

two later. Early intestinal obstruction of any variety belongs in Group 1 and is probably best treated by surgery as soon as the patient can be properly prepared.

Group 2: An example of bowel obstruction which requires immediate operation, even though the patient's condition is unfavorable, is that of strangulation. The operation should be delayed only long enough to prepare the patient for surgical intervention. This is done by an attempt to replace the water-electrolyte loss and to replenish the loss of blood or plasma. The diagnosis of a strangulated loop is made when there is intestinal colic with vomiting, intestinal distention, and absolute constipation, combined with the signs of local inflammation and peritonitis. Usually the venous rather than the arterial circulation of the bowel is disturbed. Ultimately, however, the latter is also impaired when the pressure within the vein equals the arterial pressure. However, even before this stage, there is a tremendous passive congestion which soon gives way to hemorrhage in the tissues of the intestine, then into the lumen of the intestine, and finally into the free peritoneal cavity. This initiates the so-called "aseptic" peritonitis, although bacteria are probably present. The cardinal signs of peritonitis have already been described and include tenderness, distention, adynamic ileus, and a silent abdomen. Although there are local tenderness and rigidity over the area of strangulation, these may be absent when gangrene occurs. In addition, there are fever and leucocytosis, although these are found in all types of obstruction. If in doubt, the surgeon will prepare the patient and proceed with operation immediately in all cases of suspected strangulation. Here, again, the scout film of the abdomen will be of great help in distinguishing early strangulations from such conditions as perforated appendicitis or diverticulitis, because the film will show a distended loop of small bowel, whereas in diverticulitis or appendicitis there will be an ileus of the so-called paralytic type in which both large and small intestine may be distended. In volvulus, one large distended loop may be seen. Two conditions which may be indistinguishable by physical and roentgen signs from volvulus are mesenteric thrombosis and an internal strangulated hernia.

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surgeon elect to do a complete operation in late cases, because the patient's condition will not permit it. Later he may finish his work in a deliberate manner.

Some General Rules in the Treatment of Bowel Obstruction.—From the standpoint of treatment, intestinal obstruction may be divided into four groups based upon the pathology present and the condition of the patient: (1) Obstructions which require immediate operative intervention and in which surgery may be safely undertaken; (2) obstructions requiring immediate surgery in patients whose general condition may not tolerate it; (3) obstructions in which delayed operative intervention is feasible and desirable; and (4) those types of obstruction which may be amenable to nonsurgical treatment in patients not dangerously sick. Examples of the various groups may be cited.

Group 1: Complete obstruction of the transverse, descending, or sigmoid colon must be considered as a closed loop obstruction because of the competence of the ileocecal valve on the proximal side and the presence of the obstruction distally. Therefore, this type of obstruction when complete may cause tremendous distention and must be relieved by operative intervention. The Levin or the Miller-Abbott tube with suction will be useless because of the ileocecal valve. The diagnosis of this particular type of obstruction is usually made by the history. The patient will describe successive attacks of cramping pains with a change in the habit time of bowel action, finally resulting in more or less complete constipation. Also, he may tell of alternating diarrhea and constipation, nausea but rarely vomiting, and mucus and blood in the stool. The patient is usually 50 years old or over and he does not look ill. Physical examination shows early distention, however, bowel sounds may be heard. Digital examination of the rectum will usually reveal the neoplasm. If it is too high up for the finger to feel the mass, a proctoscopic examination may be done, and this will help make the diagnosis. If the physician depends upon the patient's history or statement that he can take a large enema and, therefore, cannot be completely obstructed, he will be misled. It is true that the normal colon will accept a quart or more but usually not the obstructed one. This is, however, a debatable type of criterion because many normal patients cannot accept much water by enema. Furthermore, it is not wise to introduce too much water for fear of perforation. X-ray studies help to confirm the diagnosis. A barium enema may be tried but should not be introduced under great pressure because the barium will find its way above the obstruction where it becomes dehydrated and converts an incomplete obstruction into a complete one. The barium finally becomes extremely hard and may be very difficult to remove before surgery. A scout film of the abdomen usually reveals the greatly distended colon. The type of operation in such cases will ordinarily be palliative (that is, cecostomy or transverse colostomy) and will be a preliminary measure to deflate and empty the colon so that this organ may be removed safely a week or

already mentioned previously in this chapter the fact that bezoars may find their way through the stomach and cause an intestinal obstruction. One other type of foreign body obstruction should be mentioned which is rare, and this is an obstruction due to *gallstones*. Practically all gallstones which cause an obstruction are dislodged into the intestine through a cholecystenteric fistula. This in turn is due to a very large gallstone with cholecystitis, causing the gall bladder to adhere to the duodenum as a rule; then by pressure necrosis, the large stone is sloughed through into the small intestine. After the stone finds its way into the small bowel, it may be arrested anywhere along its course. Not uncommonly this will be near the ileocecal valve. The characteristic stages in gallstone obstruction are, first, an antecedent acute cholecystitis, chronic cholelithiasis, the passage of the gallstone through the fistula into the intestine, and then the recurrent bouts of intestinal colic and finally obstruction due to impaction of the stone. In addition, the stone, once it is lodged, begins to pick up foreign matter, causing it to increase in size, completing the obstruction. Then, of course, there is impaction behind this stone causing an obstruction. The final arrest of the stone may occur at any level of the intestinal canal, depending upon its size and the size of the bowel. Normally, however, since the lumen decreases as it reaches the ileocecal valve, the latter site will be more common. The symptoms and signs of obstruction due to gallstones are not characteristic. However, in most instances a careful history will give or reveal symptoms referable to disease of the gall bladder, usually of long duration, and the symptoms will be referable to the migration of the stone into the intestine from the gall bladder, and then there will be the symptoms and signs of recurrent obstruction. The diagnosis is rarely made prior to operation, although it may be suspected. X-ray examination reveals the site of the obstruction, the cause of which cannot be ascertained by the flat plate unless the stone is heavily infiltrated with calcium and forms a definite shadow; then it may be suspected. Rarely the x-ray film will show the air in the biliary tree, and this may help in making the diagnosis. Since barium given by mouth is contraindicated in all obstructions, the cholecystoduodenal fistula could not be visualized by this means. However, where this has been done, the fistula has been visualized.

The treatment of obstruction due to gallstone impaction is the same as that of any type of bowel obstruction; namely, a decompression with the Miller-Abbott tube. A very small amount of barium may be introduced through the tube which would lead to the site of the obstruction, should this be found necessary. As a rule, however, as soon as the distention has been removed and water and electrolytes have been replaced, operation is the treatment of choice. Enterotomy, removing the stones and suturing the bowel, gives good results. The longitudinal incision of the bowel should be adequate and be closed transversely so as not to produce a narrowing. The prognosis in the condition is usually good if the

intestine which have slipped under an adhesive band, forming a sort of pseudointernal hernia, external hernias which have been reduced enmasse, and large accumulations of pus such as in pelvic abscess and appendiceal abscess which partially occlude the bowel by extrinsic pressure.

Group 4: Obstructions which are amenable to conservative therapy are those which occur in patients who are in good general condition and who show a good response to conservative management in the first twenty-four to thirty-six hours. Such patients usually develop the obstruction in the early postoperative period. The cause is ordinarily an inflammatory edema.

The Treatment in Special Types of Intestinal Obstruction.—In addition to the rules which have been briefly reviewed, certain types of obstruction require special consideration. Atresias, stenoses, and duplications of the bowel have been considered in previous paragraphs.

Perhaps the most common type of obstruction by obturation is that of *fecal impaction.* This is seen only rarely in the normal individual, yet often enough to demand a rectal examination in every patient who has symptoms and signs of obstruction. The condition is seen not infrequently in the insane or in the aged due to the neglect of bowel function. Not too rarely, it is encountered following surgical procedures. Unless the charting is accurate, the attending surgeon may be misled into believing that the enema has been effectual when in fact it has not. The symptoms and signs are those of a low obstruction which is incomplete, and following surgery this is apt to be misleading. There is great distention and no vomiting or rarely so, and a "scout film" of the abdomen immediately shows the distended large bowel. Digital examination reveals the true condition. The treatment will require digital breaking up of the impaction and repeated use of enemas with glycerin. Very often the entire hard incretion must be removed manually, and this is particularly true in the insane. A more common type of impaction is that induced by the use of barium which has been injected beyond an incomplete obstruction due to stricture or new growth in the lower bowel. Here the barium is difficult to force through, but once it enters, it immediately or very shortly thereafter loses its fluid content and becomes hard, converting an incomplete obstruction into a complete one. It is very difficult to remove this barium. Usually a colostomy must be done to wash it out. This can be accomplished with large quantities of saline solution, and sometimes peroxide is used to break it up. Children with megacolon or Hirschsprung's disease very frequently have incomplete obstruction due to fecal impaction. This, too, must be manually extracted.

A rare form of obstruction may be due to *foreign bodies.* This is seen in the insane occasionally. It is also seen in children who have stenosis. On several occasions we have seen children with imperforate anus and rectoperineal fistula suffer complete bowel obstruction due to ingestion of a prune seed which completely occludes the small lumen to the outside. This also requires removal in order to relieve the obstruction. We have

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condition is taken care of early. The cholecystoenteric fistula should not be attacked at this time. Later it should be treated by cholecystectomy and closure of the fistula.

Intestinal obstruction due to adhesions and bands will give rise to either the simple or strangulation type. Usually if it is occlusion or compression, it will be the simple type. *Volvulus* or *torsion* may occur as a result of the presence of abnormal bands in the peritoneal cavity. In a very large series the frequency of obstruction due to bands and adhesions will equal about 30 per cent. In fact, it is now more common to find an obstruction due to adhesions or bands than to hernia. The clinical features are not unusual. The history of previous operations makes the diagnosis even more likely. If the adhesive bands simply impede the fecal current, there is very little tenderness, but if there is strangulation, tenderness is present. Diagnosis is made by the history, physical examination, symptoms and signs, and x-ray studies. It is in the immediate postoperative period that this diagnosis is particularly difficult, because it must be distinguished from an inflammatory lesion and postoperative ileus and peritonitis. Here it may be wise to use a decompression tube of the Miller-Abbott type until a diagnosis can be established. The outlook is good, and in most instances when the surgery is judicious and properly timed, recovery will follow.

Intestinal obstruction due to hernia has been discussed under complicated types of hernia. However, it should be mentioned that internal types of hernia may cause obstruction. This is particularly true of diaphragmatic hernia, hernia into the foramen of Winslow, periduodenal fossae, persistent hole in the mesentery, and other areas of internal hernia.

A volvulus or torsion of the bowel usually occurs in the sigmoid. A long flexure in which the ends of loop are closely approximated predisposes to its occurrence. It has also been reported in the ileocecal region, and in congenital types it is not uncommon. The latter have been previously discussed and will not be reviewed here. It has been our observation that any bowel that is completely obstructed and has a long mesentery may undergo volvulus due to the distention of the proximal loop which may fall in a clockwise or counterclockwise direction. We have seen this in bands around Meckel's diverticulum or in long bands due to postoperative adhesions and also in congenital types of obstruction. The clinical features are those of extreme distention. Very frequently the distended loop of cecum or sigmoid may be seen as well as percussed. Sometimes visible peristalsis is observed. The x-ray will show a large loop of distended bowel which is clearly defined and then distention proximal to this very large blind loop. In the differential diagnosis, mesenteric thrombosis, acute pancreatitis, peritonitis, and strangulation of an internal hernia may mimic the condition so closely that frequently the diagnosis is not made until operation is done. However, the local tenderness and the mass may suggest volvulus as soon as deflation has been effected by the Miller-Abbott

tube and electrolytes restored; operation should be done immediately. The mortality in intestinal torsion is about 50 per cent, and in cases requiring excision, it rises to 75 per cent. One of the reasons for this is the delay in operation. If the condition is diagnosed early and surgery instituted, the mortality is lowered. In several cases we have been able to unwind the torsion and the bowel has regained its color and did not require resection. In most instances, however, the bowel is devitalized and resection is necessary. Primary anastomosis at the time of resection may be done if the general condition of the patient permits. However, not infrequently a double barrel enterostomy will be necessary.

There are apparently two types of volvulus of the large bowel: (1) The acute type which is very fulminating and occurs in young people. It causes severe generalized cramping pain, only transient vomiting, acute distention which is great, prostration, and tenderness of the entire abdomen, particularly the twisted loop. The process is very acute and the bowel becomes gangrenous very early. (2) The subacute type which occurs in older groups of patients. The same course is present as in the acute type only it is much slower in developing. The x-ray is perhaps the best aid to the diagnosis because it shows the tremendously dilated sigmoid which, by the way, is situated on the right side of the abdomen when it twists, moderate distention of the colon above the volvulus, and the absence of collection of fluid within the twisted loop. A barium enema may be given, and this may lead to further information, although the appearance may not be entirely unequivocal. The steeple or "spire" appearance of the barium is almost characteristic. The normal appearance of the mucosa of the sigmoid and rectum distal to the volvulus is to be expected. Most patients cannot hold a large barium enema, and this in itself leads one to think of low obstruction.

Volvulus of the cecum and ascending colon is not as common in our experience. However, it does occur for the same reasons as on the left side; namely, an unusually long mesocolon. The causes of volvulus on the right side are strong peristalsis following heavy purgation or overeating, abdominal tumors, mesenteric cysts, fecaliths, foreign bodies, direct violence, habitual constipation, and, rarely, acute appendicitis. Perhaps pregnancy may be added to this list because of the position in which it places the cecum.

The diagnosis is usually not made with accuracy. However, the symptoms and signs are those of intestinal obstruction, and the roentgenological study may make the diagnosis. The cardinal points are demonstration of the dilated cecum which is enormous and variable lengths of dilated ascending colon and terminal ileum. The cecum is in an abnormal position and is found in the left upper quadrant in 90 per cent of the cases. Cecal outline is abnormal. A barium enema will enter the bowel much more readily than when the volvulus is on the left side. However, it will be found by this method of examination that the dilated portion of the large bowel is proximal to the point of obstruction and that there is no outline

of the cecum. In the differential diagnosis, the presence of obstructing tumors within the bowel, obstructing adhesions, dilated obstructed stomach, and redundancy of the colon must be considered. However, with the symptoms and signs of intestinal obstruction and the picture outlined, one suspects the presence of a volvulus which is sufficient to indicate surgery. On the left side, surgery consists of removal with primary anastomosis, if the bowel is devitalized, and if the patient can stand it; if not, exteriorization. Since volvulus tends to recur after detorsion, some method of fixation of the cecum will be sufficient to prevent recurrence. Resection is indicated where the blood supply is compromised. A simple untwisting of the volvulus on either side is perhaps unwise because of the danger of recurrence. Some method of fixation or plication is indicated. A word

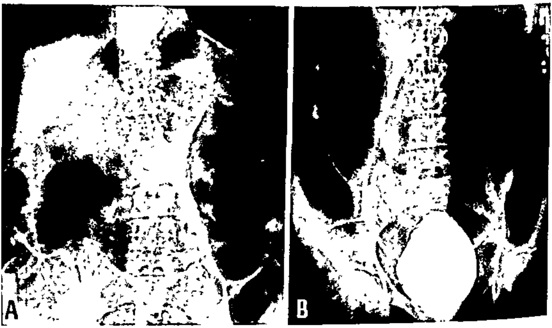

Fig 293.—Volvulus of the large intestine. *A*. The x-ray photograph is a scout film of the abdomen of a woman, 71 years of age, who came to the hospital complaining of enormous distention and constipation with some vomiting. Note the great dilation of the large bowel. *B*. X-ray photograph of a barium enema. The findings are characteristic. There is a steeple, or rather a cone outline of the superior margin of the barium. Immediately above this is the enormously dilated sigmoid. At operation the bowel was so large that a purse-string suture was placed in the serosa and a No. 18 hollow needle introduced to deflate the large intestine. After this manuever the bowel resembled a deflated innertube of a tire The purse-string suture was tied after the needle had been removed. The sigmoid had become rotated 360 degrees in a clockwise manner. Shortly after the colon had been untwisted, its color returned to normal. The patient was last seen one month after surgery and was without symptoms.

should be said about primary anastomosis. In dealing with greatly distended bowel, particularly large bowel, the danger of leak in primary anastomosis, whether it be *ileotransverscostomy or a colocolostomy*, is great, and therefore many observers have stressed the point that primary anastomosis should not be done and that exteriorization is the treatment of choice. While in principle this is true, if some form of drainage is instituted proximal to the anastomosis, we have found that this will save a second operation and will be successful in a large number of cases. In other words, it is

our practice in volvulus on the left side to do a cecostomy with a large tube to protect our suture line. On the right side the suture line is protected by temporary ileostomy made by introducing a large catheter into the ileum in the manner of a Witzel procedure. In all doubtful cases or in patients who cannot stand a primary anastomosis, a Mikulicz type of resection is the operation of choice.

Intussusception means a telescoping of one portion of the intestine or colon into a more distal segment of the enteric tube. The entering wedge is the intussusceptum and the receiving portion is the intussuscipiens. An extremely rare condition is one in which the proximal portion is the intussuscipiens. This is extremely rare. The cause of intussusception in the adult is usually brought about by some mechanical abnormality, whereas in childhood and infancy this is not true. In a large series of cases, Meckel's diverticulum, intestinal polyp, duplications, and lymphoma are found to be predisposing factors.

The types of intussusception, depending upon the anatomical position, are as follows; ileocecal, which means that the ileum is forced into the cecum (most common type), ileoileal, ileoileocecal, ileoileocolic, colocolic, and other multiple types. In other words, the intussusception may be single, double, or triple. We have had one case of triple intussusception which was ileoilealcecalcolic. The condition usually occurs in fat and healthy-appearing babies between the ages of 5 and 10 months, although it may occur in childhood or adult life. In the child the clinical manifestations are fairly pathognomonic. There will be recurrent colicky abdominal pain. This can be detected in the infant by the fact that the baby becomes intermittently pale and doubles up, drawing his legs up to his abdomen. This will last for ten to fifteen seconds, sometimes a minute. The child will burst out crying and may vomit. Indeed, vomiting is an early symptom. This recurrent pain, together with pallor, sweating, dehydration, and shock, accompanied with the passage of bloody mucus from the stool, is sufficient to make the diagnosis. Light red or dark brown mucoid material is a pathognomonic sign. If the condition is seen early, the child may appear well in between attacks of colic. However, by careful examination the mass may be felt within the abdomen or by rectal examination. Late, the child shows all the symptoms and signs of dehydration and late intestinal obstruction as previously described. Barium enema may be given and not infrequently shows the intussusception clearly. Indeed, it may partially or totally reduce it. Some have advocated this as a method of treatment. The rectal examination is important because usually bloody mucus appears on the finger and the mass may be palpated. We have had several cases in which the intussusception has proceeded so far that it could be easily felt within the rectum. This leads sometimes to the diagnosis of a prolapsed rectum. However, by passing the finger into the rectum between the intussusceptum and the surrounding anal sphincter, the diagnosis may be established. In a prolapsed rectum there is no such space to admit a finger, whereas in an intussusception this may be

of the cecum. In the differential diagnosis, the presence of obstructing tumors within the bowel, obstructing adhesions, dilated obstructed stomach, and redundancy of the colon must be considered. However, with the symptoms and signs of intestinal obstruction and the picture outlined, one suspects the presence of a volvulus which is sufficient to indicate surgery. On the left side, surgery consists of removal with primary anastomosis, if the bowel is devitalized, and if the patient can stand it; if not, exteriorization. Since volvulus tends to recur after detorsion, some method of fixation of the cecum will be sufficient to prevent recurrence. Resection is indicated where the blood supply is compromised. A simple untwisting of the volvulus on either side is perhaps unwise because of the danger of recurrence. Some method of fixation or plication is indicated. A word

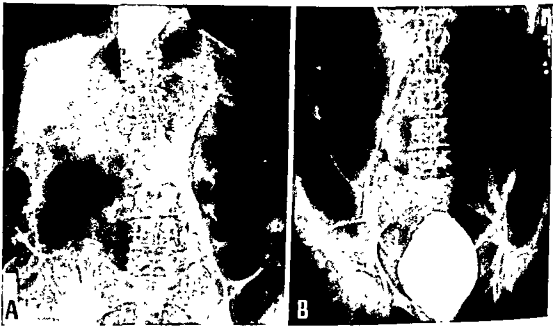

Fig. 293.—Volvulus of the large intestine. *A*. The x-ray photograph is a scout film of the abdomen of a woman, 71 years of age, who came to the hospital complaining of enormous distention and constipation with some vomiting. Note the great dilation of the large bowel. *B*. X-ray photograph of a barium enema. The findings are characteristic. There is a steeple, or rather a cone outline of the superior margin of the barium. Immediately above this is the enormously dilated sigmoid. At operation the bowel was so large that a purse-string suture was placed in the serosa and a No. 18 hollow needle introduced to deflate the large intestine. After this manuever the bowel resembled a deflated innertube of a tire The purse-string suture was tied after the needle had been removed. The sigmoid had become rotated 360 degrees in a clockwise manner. Shortly after the colon had been untwisted, its color returned to normal. The patient was last seen one month after surgery and was without symptoms.

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palpated again, where diagnosis can usually be established by feeling the mass. A longitudinal incision is made and the intussusception is reduced by the process of milking, or taxis of the proximal segment. Extreme gentleness is used so that the bowel will not be torn and so that the toxic substances are not milked out through the devitalized bowel. If it is found that the reduction cannot be effected, or if the bowel is gangrenous, resection should be done with a minimum of handling. A word of caution is necessary. After the intussusception has been reduced, the bowel wall will be edematous, and sometimes the surgeon will be misled into believing that he has effected complete reduction when another loop may be telescoped in the one already reduced. Should gangrene be present, resection is necessary and this should be done speedily and without much handling. Since the adoption of this policy, we have been successful in resecting large lengths of bowel even in very young infants where previously the mortality was extremely high, up to 50 per cent.

Intussusception in adults is known to occur through pathological influences as a rule. These may be listed as follows: typhoid ulcer, tuberculous ulcer, dysentery, acute appendicitis, Meckel's diverticulum, congenital polyp or band, submucous lipoma, foreign body, sudden dietary change, and neoplasms. Three forms are usually encountered: (1) Enteric, in which the small intestine invaginates; it occurs in older children and in adults and is usually of organic causation. (2) Colocolic, which occurs in elderly persons and not infrequently is caused by a polypoid carcinoma or benign polypoid growth. (3) Enterocolic (which accounts for 75 to 85 per cent), in which the ileum invaginates into the colon; this is not so commonly seen in adults. Following gastroenterostomy the afferent loop may telescope into the stomach or the afferent loop may find its way into the stomach by retrograde pulling up or by the stomach falling down over it. Thus, either of the loops may intussuscept into the stomach.

The symptoms and signs in adults are very vague since the obstruction is not complete. There are colicky pains in the abdomen, some nausea and vomiting, constipation, and blood stools. A mass may be felt, but only in very thin individuals. The diagnosis is made mainly by barium enema, and not infrequently barium is given by mouth with the supposition that the obstruction is partial. The differential diagnosis in children lies between acute appendicitis, acute enterocolitis, simple colic, mesenteric lymphadenitis, and tuberculous mesenteric lymphadenitis. In the adult, as in the child, operation is indicated. If reduction is easily accomplished, this may be all that is necessary. However, should the blood supply of the bowel be impaired, resection must be done. It does not carry the high mortality that the same operation carries in children, provided that the operation is done early and that the patient is properly prepared for surgery.

Obstruction Due to Vascular Lesions.—This type of obstruction may be due to mesenteric thrombosis or embolism. The arterial occlusion is

traced as high up as the finger can reach. Usually there is no fever in either case. The barium enema shows an obstruction with a cupola effect; a thin cylindrical shell of barium surrounds the intussusception which remains after evacuation of the enema; and there is a partial or complete regression of the intussusceptum if the barium is injected with sufficient pressure.

The *treatment* of the condition is immediate operation. Although some observers still believe that the barium enema is useful in reducing the obstruction, we have considerable doubt about this method because one cannot be sure that the entire intussusception has been released. It is therefore proper to conclude that barium enema should be used for diagnosis rather than for treatment. The patient should be prepared the same as in other type of intestinal obstruction, and under ether anesthesia the abdomen

Fig. 294.—Triple intussusception. J. D. was a boy 7 months old, who came to the hospital with a history of cramping pains in the lower abdomen accompanied by the passage of a small amount of bloody mucus. The mother stated that the child had vomited at frequent intervals and that he was quiet for periods varying from ten to thirty minutes, then he would suddenly cry out and draw up his legs as though he were in violent pain and pass a little bloody mucus. The x-ray photograph shows the preoperative condition. At operation a triple intussusception was encountered. The first occurred about 12 cm. from the ileocecal valve. This was an ileo-ileal intussusception. This, then, pushed its way into the cecum, forming an ileo-ileocecal intussusception (white arrow). In turn, the cecum invaginated into the ascending colon, converting the intussusception into an ileo-ileocecal-colic intussusception (black arrow). At operation the three intussusceptions were reduced by the retrograde "milking" technique. Fortunately, no gangrene was present and the child made an uneventful recovery. (Case referred by Doctor H. Call.)

thought to be the cause of 60 per cent and thrombosis of a vein in 40 per cent. However, regardless of the type, after the obstruction is established, both components become occluded. The superior mesenteric artery is more frequently concerned in embolism than the inferior, partially because of its earlier exit from the aorta, but mostly because it is of more direct continuation. Furthermore, it is important that in inferior mesenteric thrombosis due to a better and freer anastomosis which occurs between the end vessels, occlusion of the vessel may fail to produce gangrene. Last, thrombosis of the portal vein may cause a type of infarction of the upper bowel, including the stomach. We have recently encountered two cases with thrombosis of the celiac axis in which the hepatic artery was involved. Vegetations on the valves of the left side of the heart are usually the etiological factor. However, this is not uniformly true. The causes of embolism as previously described may predispose to mesenteric thrombosis. In addition, such conditions as arteriosclerosis and thromboangiitis obliterans have been reported. We have had one case of the latter. This was present in a patient who did not have peripheral Berger's disease. The aching, gnawing periumbilical pain was always exaggerated after a meal when it became so severe that we termed it "intermittent intestinal claudication." Last, we have recently reported a case in which we think

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and was dismissed from several hospitals because there could be found no actual cause for his excruciating pain. Finally, he was thought to be a morphine addict.

On admission to the hospital he had a temperature of 101.4° F. with a pulse of 100 and respirations of 25. The systolic blood pressure was 130 and the diastolic was 70. The entire abdomen was soft, but the patient complained of severe pain. The lower abdomen seemed to be more full than the upper, and there was some tenderness in the region of the left costovertebral angle. Physical examination disclosed no gross abnormalities. Some significant laboratory tests should be mentioned. The white blood count was 40,100. The urine had a specific gravity of 1.033 and had albumen and ten to fifteen pus cells per high-power field. The P.S.P. kidney function test of two hours was 55 per cent. The spinal fluid examination was normal. This patient became steadily worse and the generalized abdominal pain finally was so excruciating that a grain of morphine failed to relieve it. The patient was vomiting. At this time surgical consultation was requested and a diagnosis of mesenteric thrombosis was made. However, before surgery could be instituted the patient expired.

Post-mortem examination showed the peritoneal cavity to contain a small amount of brownish fluid. The small intestines were distended with gas and were necrotic. There was a small amount of fibrinous exudate on the peritoneal surfaces. The necrosis extended from the duodenal jejunal flexure to within 20 cm. of the ileocecal juncture. The cause of this thrombosis is extremely interesting. *A.* Proximal portion of the superior mesenteric artery hematoxylin-eosin stain. The dark area in the center is a fresh thrombus. *B.* Proximal portion of the superior mesenteric artery elastic tissue stain. Dark area in center is fresh thrombus around which is a pale vascular fibrous tissue (old organized and canalized thrombus or possibly thickened intima.) At the upper right inside the internal elastic lamella is a crescent-shaped dark area composed of fibrous tissue containing many elastic fibers (which stain black). The crescent-shaped area may be a thickened intima or an older organized thrombus. *C.* Cross section of the aorta showing a plaque in the intima. Note the pale lipoid areas in the depths of the plaque and the dark-staining, fresh, organized thrombus on the surface. *D.* Aorta with many plaques. Note the large pale lipoid area in the plaque on the right and thrombus on the surface of plaque on the left.

This illustrates a case of internal thromboangiitis obliterans. There was no evidence of the disease in the extremities either clinically or at post-mortem examination. This case exemplifies many well-known clinical features of mesenteric thrombosis, but by far the most important feature is pain out of all proportion to the physical findings. The radiation and location of the pain did not fit any other clinical picture and as in thrombosis anywhere in the body, the pain is severe but particularly so when the mesenteric vessels, either arterial or venous, are occluded. The pain may be compared to that of an acute hemorrhagic pancreatitis and, indeed, can only be distinguished clinically from this by the presence of bloody stools in mesenteric thrombosis. Another feature of this pain is the fact that it occurs in characteristic episodes before it finally becomes continuous. Undoubtedly, the episodes of pain are due to vasospasm before the occlusion is complete. This is aggravated by increased peristalsis after eating very much, as *intermittent claudication* is brought on by muscular activity in peripheral vascular disease. Obviously, when the blood supply is completely shut off, the pain is continuous and excruciating. (Berman, J. K., and Thornton, J. C.: J. Indiana M. A. 33: 138, 1940.)

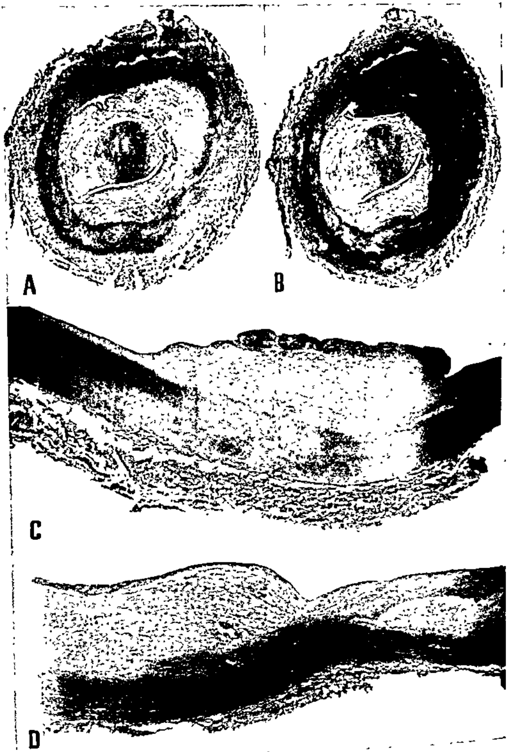

Fig. 295.—Occlusive vascular *disease of the abdomen.* The cause of mesenteric thrombosis is discussed in the text. However, a rare cause is that of occlusive vascular disease similar to some of the varieties which are found in peripheral vascular disease discussed in Chapter 6. The patient whose vessels are shown in the photomicrographs was a white man, 38 years of age, who came to the hospital complaining of a severe generalized, constant abdominal pain, made worse by the ingestion of food or water. He had attacks of vomiting, pain in the scrotum, burning on urination, and constipation. He had been sick for about seven months; however, x-ray examinations and careful studies failed to reveal the cause of the severe pain. He was diagnosed as a psychoneurotic

(Continued on opposite page)

that large doses of ergot predisposed to an endarteritis affecting the mesenteric vessels. In this patient, a thrombosis of the superior mesenteric artery occurred following the ingestion of large quantities of ergot. Embolism is more frequent than thrombosis of the artery. Venous thrombosis is usually associated with an infection within the abdominal cavity, such as appendicitis, strangulated hernia, septic pylephlebitis. Should obliteration of the mesenteric artery occur slowly, it is conceivable that a collateral circulation could be formed and that gangrene would not occur. The condition may be diagnosed by the symptoms and signs. Usually the patient complains of severe abdominal pain which comes on suddenly. There is vomiting in large copious amounts of dark, bloody fluid. If the inferior mesenteric artery is involved, a diarrhea may occur with large amounts of blood. This will not be true until late if the superior mesenteric artery is involved. Shock is usually present, and distention of the abdomen is progressive and the bowel sounds are absent. The pain is extreme. In no condition is pain more severe than in that of mesenteric thrombosis, not even the pain of acute hemorrhagic pancreatitis. There is a high leucocytosis. The flat plate of the abdomen shows the distended loops of bowel which are widespread and which give the idea of a paralytic ileus rather than a mechanical obstruction. Therefore, in patients with predisposing causes, such an endocarditis or inflammatory lesions within the bowel, the sudden onset of pain with distention and vomiting of blood-stained fluid in large quantities, silent abdomen, bloody diarrhea if the inferior mesenteric artery was involved, together with no fever, shock, the distended bowel as seen by x-ray all point to the diagnosis of mesenteric thrombosis. The *treatment* is *immediate surgery*. Large amounts of intestine may be *successfully resected with primary anastomosis. There should be careful* attention to water balance and blood volume balance, and it is our opinion that chemotherapy aids in the protection of the patient against peritonitis. Therefore, large doses of penicillin and streptomycin are used. We have recently reported a case in which we resected 216 inches (549 cm.)—539 cm. of small intestine and 10 cm. of large intestine.

Neoplasms of the small bowel rarely cause an obstruction. The neoplasms may be benign or malignant. The benign types include lipoma, myoma, adenomyoma, fibroma, adenoma, angioma, various types of cysts and polypi, and heterotopia of gastric, pancreatic, and other types of tissue. The importance of these benign tumors is that they very often start an intussusception. Sometimes they cause bleeding, particularly the angiomas. There may be colicky types of pain, and the diagnosis may be made by a careful examination by barium meal. However, usually the diagnosis is established at operation. Of the malignant types of growths in the small bowel, multiple carcinomas have been reported; also polypoid carcinomas, exclusive of the ampulla of Vater. Adenocarcinomas are sometimes found in the duodenum, the jejunum, or ileum. In addition, sarcomas, carcinoids, primary Hodgkin's disease, atypical reticuloendotheliomas, lymphosarcomas, and neurogenic sarcomas have been reported in the

Fig. 296.—Mesenteric artery thrombosis. Photograph of gross specimen of resected intestine which included the entire small bowel except for about eighteen inches (45.7 cm. of jejunum). The rest of the bowel, including the remainder of the jejunum, that is, all except eighteen inches, all of the ileum, the cecum, and ascending colon, were removed up to the hepatic flexure, and then the jejunum and transverse colon were anastomosed by a side-to-end anastomosis. Arrow points to thrombus in the superior mesenteric artery. L. B. was a woman, 51 years of age, who came to the hospital complaining of severe abdominal pain with continual epigastric cramping pain which radiated to the lumbar area, vomiting of copious amounts of thin, dark, foul-smelling grumous fluid. The abdomen was distended and a few tinkling sounds were heard on auscultation. Rectal examination did not show any abnormalities, and blood was not seen on the examining finger. The leucocyte count was 16,400. A roentgenogram of the abdomen revealed great distention of the stomach and multiple distended loops of small bowel with some distention of the colon. The excruciating pain, the high leucocyte count without fever, the suddenness of onset, lack of previous surgery, the type vomitus, the shock all pointed to a mesenteric thrombosis, and since there had been no passage of bloody material from the rectum, it was probably in the superior mesenteric rather than in the inferior mesenteric distribution. This was found at operation. The patient made an excellent recovery and was last seen in July, 1949. At this time she was still having approximately six to eight pasty stools per day. However, they had decreased in amount and the consistency was becoming more firm.

Recently the patient returned to the Indianapolis General Hospital for study. The following significant findings were present. (1) Although the patient was hypertensive before surgery, her blood pressure is now normal. (2) There is no free Hcl in the stomach. (3) There is a severe hypochromic microcytic anemia (4) There has been complete amelioration of symptoms with the use of B_{12}. (From Berman, Brown, Foster, and Grisell: J. A. M. A. 135: 918, 1947.)

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small intestine. Diagnosis is usually established at the time of operation, although in cases which have a long history of colicky pain and in which no definite diagnosis can be made, a careful examination with the x-ray should be done. If this does not reveal the site of obstruction or the cause for the colicky pain, it may be necessary to do an exploratory operation with stripping of the bowel in an effort to locate the site of the growth. In benign or malignant neoplasms the growths should be removed, the former by enterotomy or resection, depending on whether the neoplasm is on a pedicle or is sessile, and, of course, in malignant types, resection with an adequate margin of normal tissue and with associated lymph nodes should be done. Sarcoidosis of the small intestines may simulate nonspecific types of enteritis or benign growths or malignant growths. *This is known as Besnier-Boeck-Schaumann disease.*

Jehgers and co-workers have recently reported a new syndrome which is recognized by two features: (1) melanin spots of the buccal mucosa and lips (sometimes also the face and digits), (2) polyposis (adenomatosis and papillomatosis) of the small intestine (rarely the stomach, colon, and rectum). The disease seems to be hereditary.

Other causes for obstruction may be due to *inflammations*. Of these the more common are tuberculosis and regional enteritis.

Adynamic Ileus.—True or idiopathic postoperative paralytic ileus is rare and is probably a misnomer because (1) it is not a true paralysis since the Miller-Abbott tube will go down, and (2) it is rarely, if ever, idiopathic. It may be associated with any type of obstruction and is usually the end stage in all obstruction. The causes of adynamic ileus are as follows:

I. Intra-abdominal
- A. Peritoneal irritation
  - 1. Traumatic
    - a. Postoperative
    - b. Penetrating wounds
  - 2. Bacterial: peritonitis
  - 3. Chemical
    - a. Extravasation of blood
    - b. Perforated peptic ulcer } Early
    - c. Bile peritonitis } Early
    - d. Acute pancreatitis } Early
- B. Vascular changes
  - 1. Strangulation
    - a. Intramural: distention following mechanical ileus
    - b. Extramural: compression of the mesenteric vessels
  - 2. Mesenteric thrombosis
  - 3. Abnormal permeability of capillaries—angioneurotic edema
- C. Extraperitoneal irritation
  - 1. Hemorrhage, especially retroperitoneal
  - 2. Infection
  - 3. Renal

II. Extra-abdominal
  A. Toxic
    1. Pneumonia
    2. Uremia
    3. Empyema
    4. Systemic infection
  B. Neurogenic
    1. Injuries and diseases of the spinal cord
    2. Lead poisoning
    3. Fracture of the lower ribs

The symptoms and signs include vomiting, constipation, great distention, "silent" abdomen, with or without tenderness, depending upon the cause, but with little pain. X-ray examination shows all of the bowel to be distended. Although the picture resembles peritonitis as previously described, there are differences in the so-called "idiopathic" type. There is absence of fever and leucocytosis; vomiting occurs in large quantities, yet there is expulsion of gas and even a mild diarrhea. Mental symptoms are common. There is severe dehydration and hypoproteinemia.

The treatment includes prevention—no strong cathartics preoperatively and during operation gentle handling of tissues, careful hemostasis, peritonealization; postoperatively, liquids only for forty-eight hours, minimal use of narcotics, early mobilization (which implies early and adequate urination without use of the catheter), no cathartics and no enemas until bowel action has become coordinated (about fourth day). The treatment consists of passage of the Miller-Abbott (and not the Levin) tube with suction, attention to electrolytes, water, protein, and blood volumes, and oxygen inhalation. In addition, careful examination to determine the probable cause of the ileus must be done. We have found that as long as the bowel remains distended, it will be difficult to restore water and electrolyte balance. Therefore, the Miller-Abbott tube must be used early. Enterostomy is not as effective but may be employed if the Miller-Abbott tube cannot be introduced. The tube should remain down until there are good strong bowel sounds, complete deflation, and normal passage of gas. Then the tube should be removed slowly over a period of at least forty-eight hours; x-ray studies with the tube in place may disclose the site of obstruction.

Multiple Causes of Obstruction.—In any bowel obstruction there may be many causes rather than one single factor. Although a list of causes are given, it is common experience to find more than one lesion or even more than one lesion of the same kind; for example, bands with volvulus, multiple tumors, appendicitis with pelvic abscess, strangulated hernia (postoperative) with bands inside the abdomen also obstructing, etc.

Rupture of the intestine may occur without external wound, simply from blunt force. Punctured wounds, made by bullets or sharp instruments, may cause a perforation. Perforative peptic ulcer may cause a leak in the stomach or duodenum. In any of these the primary peritoneal

insult may cause shock. This is followed by *violent pain, with boardlike rigidity of the abdominal muscles.* The x-ray may reveal free air between the liver and diaphragm. Unless immediate operation with closure of the perforation is done, peritonitis will result. Multiple perforations due to gunshot are better treated conservatively. Closure of all is almost impossible without endangering life. Nature effectively seals these small holes in most cases. If hemorrhage is a complication, the outlook is not as favorable.

Tuberculosis occurs usually in the lower ileum, attacking Peyer's patches of lymphoid tissue. Although a mass of tissue may be felt, usually the symptoms are those of tuberculosis plus intestinal obstruction (Chapter 8.) The treatment is surgical and consists of resection of the diseased bowel and ileocolic anastomosis. Typhoid fever also attacks Peyer's nodules. Sometimes severe hemorrhage or perforation occurs in typhoid, demanding surgical intervention.

Terminal ileitis (regional enteritis, nonspecific granuloma) occurs in the small intestine (lower ileum), although a similar lesion may occur in the colon (regional colitis). Rarely more than one side is affected at the same time. The lesion is inflammatory, begins and ends abruptly in the bowel, and may give rise to localized abscesses, due to penetration of the bowel wall. Fistulae may result. In the early stage there are swelling and edema, with regional lymphadenitis. Later, fibrosis occurs, with obstruction. The cause is not known. The disease may be related to lymphogranuloma inguinale, although there is no proof of this, which produces strictures in the rectum, or, like cardiospasm, it may be due to overactive sympathetics, with local spasm and ultimate fibrosis. There is evidence along this line because of the type person who usually contracts the disease. The so-called linear type is defined in Chapter 10 in which peptic ulcer or chronic ulcerative colitis as well as regional enteritis may be present. Symptoms are variable. They may resemble acute appendicitis or may be vague abdominal pain with alternating attacks of diarrhea and constipation. Diagnosis is made by fluoroscopic examination with barium enema. This shows a characteristic narrowing of the ileum (string sign). Other parts of the small or large bowel show deformities which involve fairly long segments. Treatment in the early stages may be palliative and includes the use of penicillin and streptomycin with succinylsulfathiazole or Sulfathalidine. Psychotherapy helps. The lesion may be discovered first when the surgeon removes a supposedly diseased appendix. Sometimes resolution occurs following this procedure; more frequently, resection is necessary, but is not always curative. Indeed short-circuiting operations may give the same results as resection, although the latter is preferable.

Appendicitis

The most common surgical condition encountered in the hospital is *appendicitis.* This is an inflammation of the vermiform appendix caused

by infection, obstruction of its lumen, or obstruction with infection. Obstruction is probably the deciding factor in every case. This may be edema, mucous fecalith or lymphoid hyperplasia, scarring or mechanical twist. In any event, there is created a blind loop obstruction which interferes with venous return, causing more obstruction. Soon the venous pressure *equals arterial pressure, and gangrene with perforation may result and* may be followed by peritonitis or abscess (local pelvic, subphrenic pericolic, or horseshoe which extends across the pelvis and up the right and left colic gutters). Seepage of contaminated fluid may occur through the appendix wall due to great intraluminal tension in addition to the devitalization without actual perforation, thereby accounting for abscess and peritonitis without perforation; if the obstruction is evolved slowly or if the secretory power of the appendiceal mucous membrane is impaired, atrophy takes place.

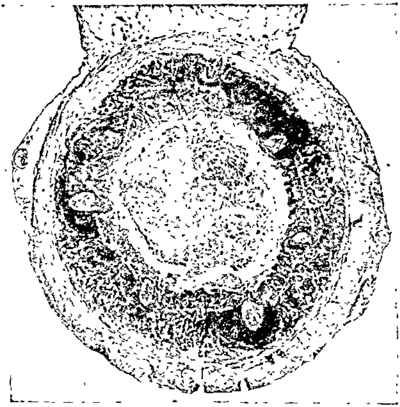

Fig. 297.—Acute appendicitis. The mucus membrane is swollen and filled with leucocytes and dilated capillaries. All coats are edematous. Early stage.

Abscesses may occur in the following positions: ileocolic, retrocecal, pericecal, pelvic, subhepatic, subphrenic, left colic, horseshoe abscess. This is especially true if a strong purge has been given, increasing peristalsis and intraluminal pressure. The appendiceal vein is thrombosed early and a septic pyelophlebitis with multiple liver abscess may ensue. The *cause*

is unknown. However, various factors play a role; namely, the seasons fall and spring with upper respiratory infections and lymphoid hyperplasia, position (retrocecal) with mechanical obstruction, familial tendency.

Symptoms and Signs.—Since the appendix in children has a large amount of lymphoid tissue, this becomes swollen when there is a cold or sore throat through the action of the same virus that invites inflammation in the lymphoid tissue of the pharynx, tonsils, and cervical lymph glands. Hence, a cold with pain in the abdomen may be misleading. Appendicitis begins with pain in the upper abdomen or around the umbilicus; then, as it develops, the pain localizes at the site of the inflamed appendix, which is usually, but not always, at McBurney's point. The difference in symptoms in appendicitis is due, in a great measure, to variations in the position

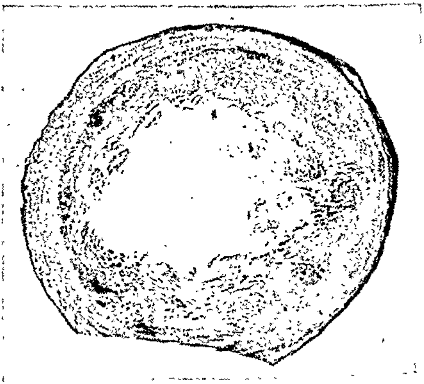

Fig. 298.—Gangrenous appendicitis. The mucosa has been destroyed. The site of perforation would probably have been at the lower portion, for here all layers are necrotic.

of the appendix. It will be low in the pelvis in the individual of the linear type with visceroptosis and high in the lateral type. Sometimes it lies under the liver when the cecum remains in the fetal position. Since the disease is rapid in its progress, it either subsides (resolution or release of obstruction), or goes on to suppuration, or even to perforation, within twenty-four to forty-eight hours. Therefore, *any abdominal pain, with or without vomiting, must be considered appendicitis until proved otherwise.* The diagnosis is made from a history of pain and constipation (if no cathartic has been taken). Cathartics should never be used in children with abdominal pain. There are tenderness and rigidity over the appendix.

The pain may be increased if the appendix is retrocecal by elevating the leg and keeping pressure over it, causing contraction of the iliacus muscle, or by turning the patient partially on the left side and making lateral pressure. Rectal examination is done especially in children, for the entire pelvis can often be felt, including the inflamed appendix, if it is in the normal position. Vomiting is almost universal in appendicitis in children. Bowel sounds are diminished in appendicitis, increased in early peritonitis, absent in late peritonitis. In women, vaginal examination is made to rule out adnexal or pelvic disease. There is very little fever at first. Should suppuration or perforation or pylephlebitis occur, a septic temperature may appear. The leucocyte count is usually elevated. However, it may be normal even in perforated appendicitis and is therefore interpreted as one of the symptoms. The urine must be examined to rule out pyelitis or diabetes, either of which may cause comparable symptoms. X-ray examination is not done routinely, but in doubtful cases it may show a basal pneumonia or free air in the peritoneal cavity. More important is the fact that gas is usually present in the cecum and practically always present in the cecum in appendicitis. A flat x-ray plate of the abdomen will, as a rule, reveal the position of the cecum and show the surgeon where to make the incision, whether high (in the fetal position), low in the pelvis, or over McBurney's point. The x-ray is not useful in diagnosing appendicitis per se, but it does help to rule out other conditions (such as kidney stone and perforative ulcer) and demonstrates the *location of the cecum*, to which the appendix is always attached. Differential diagnosis includes the following conditions: (1) In children, mesenteric lymphadenitis (often in upper respiratory infections mesenteric lymph glands will be involved, giving rise to symptoms that resemble appendicitis; microscopic study of such glands shows them to be the site of a nonspecific inflammation; for unknown reasons, appendectomy frequently relieves the symptoms); pyelitis and "idiopathic" peritonitis (usually in girls); bronchopneumonia; acute enteritis; rarely, anomalies of the right ureter, regional enteritis, and Meckel's diverticulitis. In adults the above conditions plus pelvic disease in the female, ureteral stone, gall bladder disease, and perforated peptic ulcer. *Operation is indicated as soon as the diagnosis is made.* There is no other treatment. The revered ice bag simply masks symptoms by its analgesic action and invites gangrene by vasoconstriction. Heat is preferable because it hastens localization while the diagnosis is unestablished, but heat does not cure appendicitis. The appendix should be removed through a McBurney (muscle splitting) incision. (See discussion under peritonitis.) The stump of the appendix is inverted by purse string after location and cauterization of the stump or by inversion as in any bowel suture. Peritonealization is very important and should be done unless the cecum is acutely inflamed. Here the appendix is ligated and soft drains are inserted down to it so that if a fistula results external drainage will follow. If the cecum is edematous, appendectomy is useful, provided too much manipulation is not done to accomplish it. Appendiceal abscess

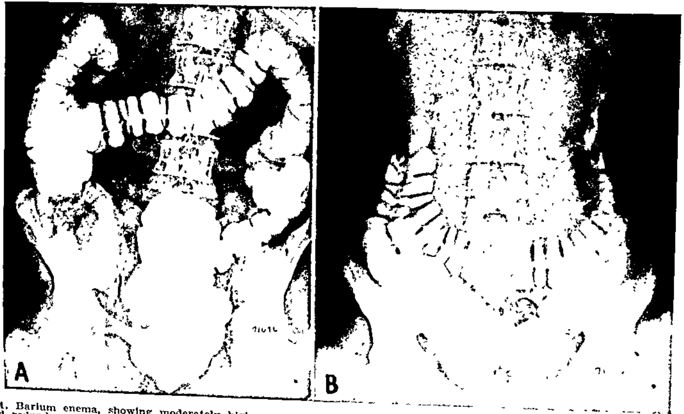

Fig. 299.—*A*. Barium enema, showing moderately high cecum at about the level of the crest of the ilium. *B*. Barium enema, showing very low cecum and redundancy of transverse colon. The position of the cecum is important in the diagnosis of appendicitis. It is not good practice to introduce a barium enema in suspected appendicitis. However, a scout film may be made which will show the distended cecum and show its position; then if the clinical symptoms and signs correspond to the position of the cecum, the diagnosis is more certainly established and, what is more important, the proper position for the incision is easily determined. The cecum is distended with gas in the presence of an inflammatory lesion because it loses its propulsive power. The barium enema shown in *A* reveals a cecum which is slightly higher than normal and has not descended to its normal position. *B* shows a cecum which is low, but the transverse colon is also low. This position is apt to give rise to symptoms which are those of an incomplete obstruction. Very often after pelvic operations the surgeon will place the greater omentum down in the pelvis and drag the transverse colon with it. This practice sometimes leads to a low position of the transverse colon with partial obstructive symptoms.

requires drainage, and in most cases appendectomy can be done but not if the appendix is part of the abscess wall. Simple drainage is safe, and later the appendix can be removed and with surprisingly little difficulty. The question of drainage in general peritonitis is a moot one because drains do not evacuate the entire peritoneal cavity and are soon isolated; in addition, there are foreign bodies. However, if placed where pools of exudate collect (pelvis, right colic gutter, and right shoe fossa), they will at least empty these pockets temporarily of material that would otherwise have to be absorbed. The drains are soft Penrose drains and are never placed among coils of intestine. If the exudate is clear and a good inversion of the cecum is possible, drains are not used (See discussion on Peritonitis.)

Recurrent Appendicitis

Recurrent appendicitis is due simply to repeated temporary obstruction to the lumen of the appendix by edema, hyperplasia of appendiceal lymphoid tissue, or fecalith, resulting in thickening and fibrosis. The appendix does not act as a focus of infection but may interfere with the mechanical movements of the gastrointestinal tract, causing "indigestion" and even vomiting, and for this reason it should be removed.

Nonspecific Types of Appendicitis

The appendix is sometimes inflamed by parasites such as the *pinworm* or the *Oxyuris vermicularis*. This may have its effect by causing an obstruction or by producing an irritation within the appendix. It cannot be diagnosed preoperatively. However, a high eosinophil count, together with the symptoms and signs of appendicitis, may give a clue. In addition to parasitic infestations, fungus infection such as *actinomycosis* may cause appendicitis. Indeed, a diseased appendix is the site of the primary focus in most cases of abdominal actinomycosis. This has been discussed in Chapter 7. The diagnosis again is made at the time of the operation. This is one of the reasons that all appendices removed should be carefully examined by the pathologist. The treatment of actinomycosis, once the appendix has been removed, consists of potassium iodide and thymol and the use of sulfadiazine as well as penicillin.

Neoplasms in the appendix include the myxomas which may give rise to a pseudomyxoma peritonei. In addition and perhaps the most important of the tumors found in the appendix is a group known as paraganglioma or carcinoid tumors or argentaffine tumors. These growths get the name carcinoid because they resemble carcinoma. The mass of paraganglioma cells invades the submucosa. The cells come from the chromaffin system and therefore belong to the paraganglioma groups. They occur twice as frequently in the appendix as in the small bowel, although they are seen uncommonly in all of these locations, including the large bowel. There have been cases reported in the stomach and even in the rectum. The diagnosis is never made preoperatively because the symptoms and

signs are those of appendicitis. When the appendix is removed, the carcinoid tumor is found. In the small intestine the tumor may produce diarrhea with or without bleeding. The appendicitis which accompanies the tumor is probably due to obstruction. Usually the growths are benign; however, we have seen several cases with metastases to the regional lymph nodes and even to the liver. The treatment is complete removal, and if it is suspected at the time of operation, a more radical resection of the mesoappendix and adjacent structures, including the lymph nodes, is practiced.

Lastly, adenocarcinoma of the appendix has been reported. This is a rare condition and again cannot be diagnosed preoperatively. A more common condition which is very important and which we have observed on several occasions is acute appendicitis associated or rather as a complication of carcinoma of the cecum. It is therefore proper to make a careful examination of the cecum at the time of appendectomy. The diagnosis having been made by surprise, the operation would be of the Mickulicz type of resection. Although this discussion would lead the reader to believe that it would be sheer carelessness if carcinoma of the cecum were overlooked, yet occasionally there is an acute suppurative appendicitis even with abscess superimposed upon a carcinoma of the cecum. This makes diagnosis very difficult. Every bit of tissue should be sent to the laboratory, and this is another reason for insisting on routine laboratory examination and microscopic study of every bit of tissue removed at the time of operation.

THE COLON

There is no digestion in the large bowel. The fecal current is liquid at the cecum and solid in the sigmoid.

Many toxic substances are formed in the large bowel as a result of the decomposition of protein by the normal bacterial flora. However, absorption of such products does not occur if the mucous membrane remains intact. The so-called "toxic" symptoms resulting from constipation have been produced by mechanical distention of the large bowel with balloons. Three types of motion are seen in the large bowel: (1) retrograde waves (most common in the ascending colon) which favor absorption; (2) coordinated waves in which haustrations disappear; (3) powerful waves of the left colon of which the individual is aware and which help in defecation. Since the patient is unaware of (1) and (2), a disease such as carcinoma gives few symptoms when it occurs on the right side, more when it is on the left side.

Continual spasm may occur at various sites in the alimentary canal, the cricopharyngeus muscle, the cardia and pylorus of the stomach, the ileocecal valve, the iliac and pelvic colon, and the anal sphincters, the large bowel, and the rectum.

Congenital Anomalies

Anomalies of the large bowel roughly mimic those that occur in the small intestine. The malrotations have been discussed in previous para-

graphs. There remains a group of congenital anomalies or anomalies which may be related to congenital defects that may be discussed here:

Atresias and Stenoses.—Most atresias and stenoses of the large bowel occur at the distal end; namely, in the hind-gut, where it joins the proctodeum. These will be discussed in subsequent paragraphs. There are other sites, however, in which atresias and stenoses may occur. The most common of these is in the middle of the transverse colon. This is due to the fact that the mid-gut in its earliest development is a convex loop with its end attached to the duodenocolic isthmus and is supported

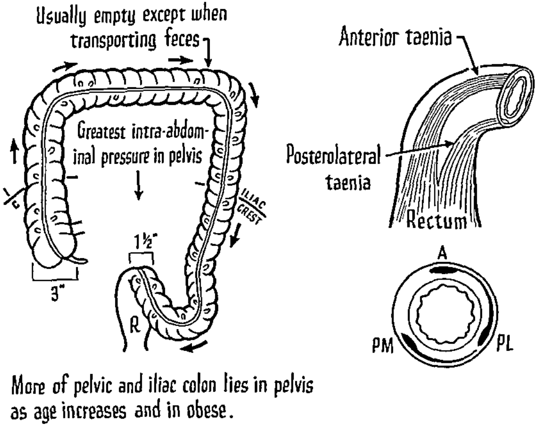

Fig. 300.—Anatomical peculiarities of the large bowel are illustrated in this figure. On the left the large bowel is shown to be roughly a cone with its wide part at the cecum and its narrow part at the rectosigmoid junction. Upper right, the taeniae are shown to expand as they approach the rectum, completely encircling the bowel at this point. Lower right, the lower portion of the pelvic colon is devoid of longitudinal muscle over a small area on either side. *A*, anterior taeniae; *PM*, posteromedial taeniae; *PL*, posterolateral taenia.

through its length by common dorsal mesenteries. At this site, which approximately corresponds with the left half of the transverse colon, atresias and stenoses may occur. Far more common, however, are the atresias and stenoses of the hind-gut close to the point of fusion with the proctodeum. The hind-gut at its distal end may remain blind or may be stenotic for a distance of 5 or 6 cm. The symptoms and signs of atresias of the large bowel are very much like those of imperforate anus and will be discussed later. In general, however, vomiting is late, distention is early, and the

x-ray film reveals not only small but large bowel dilation. At operation a thorough search should be made for the point of obstruction, and then the surgeon must satisfy himself that there is only one stenosis or one site of atresia. Primary anastomosis can be done if sufficient bowel remains below the site of obstruction. In the extremely low cases, such as occur in the pelvic colon or the iliac colon, a colostomy must be done with the thought in mind that at a later date the large bowel may be brought down to the patent rectum and anastomosed. Although babies stand enterostomy poorly, they do stand colostomy well if attention is given to water balance and blood volume replacement.[7]

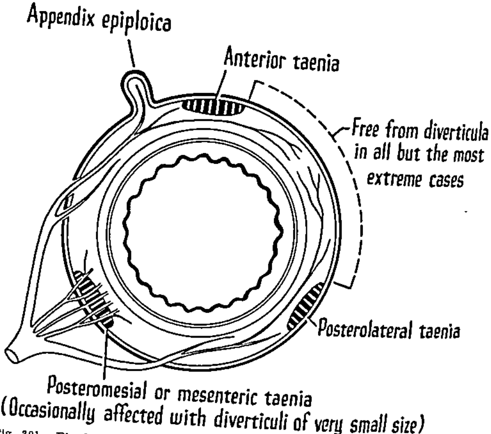

Fig. 301.—Blood supply of large intestine. Diagram illustrating the blood supply of the large intestine and the areas which are predisposed to the formation of diverticula. The blood vessels of the large bowel enter from the mesentery along with mesenteric side of the lateral and medial posterior taeniae and also with some small vessels between them. Since the longitudinal muscle is incomplete, the vessels lie rather superficially between the posterior and anterior longitudinal bands beneath the serosa. This accounts for the enormous distention which is possible in the large intestine without complete interference of the blood supply as compared with the relatively small amount of distention tolerated in the small bowel where the vessels are covered by both circular and longitudinal muscles. (From Berman, J. K., and Bower, T. B.: J. Indiana M. A. 35: 197, 1942.)

Duplications of the Large Bowel.—Duplications, as we have seen, may occur anywhere along the gastrointestinal tract. We have encountered two cases of duplications of the pelvic colon. Cases are on record of duplication of the entire large bowel, including the appendix. Even triplications are on record. Our diagnosis at first was that of a mesenteric cyst. Careful examination, however, revealed this to be a duplication. In

neither instance was it necessary to resect the colon. If the blood supply to the duplication and the bowel are one and the same, it may be necessary to do a resection. We have also encountered a duplication of the rectum. This presented itself as a pararectal cyst. Upon microscopic examination it was lined with a mucous membrane, characteristic of the large bowel. This was removed and was entirely separate from the rectum. In all duplications the diagnosis is greatly facilitated by the use of barium enema, and in duplications of the pelvic colon and rectum an anterior meningocele or a sacrococcygeal tumor presenting anteriorly must be borne in mind. A barium enema will outline this, at least giving the surgeon a clue as to the nature of this pathological entity. Two facts must be borne in mind in all duplications; (1) The intimate relationship of the duplication and the parent bowel. If it is small, it does not present much of a problem to remove the duplication, the point of contact being resected and turned in. If the relationship is extensive, resection of the duplication as well as the parent structure will be necessary. (2) The blood supply. Many times the vessels are contiguous, coursing over the duplication in such a manner that removal of the duplication cannot be accomplished without interfering with the blood supply of the parent structure. This, too, will demand resection.

Malrotation.—Malrotation of the large bowel has been considered in connection with a discussion on malrotation of the small intestine. It remains for us briefly to outline the more common abnormalities which may be encountered.

The position of the large bowel may be abnormal. The cecum, for example, may be found in the left upper quadrant with the ileum entering from right to left. The cecum with its attached appendix may also be found in the right upper quadrant, having remained in a fetal position. From here it may be found in any position, including the pelvis. Also it is common in the newborn to find the sigmoid in the right side, entering the pelvis from right to left. Later the sigmoid rotates over to the left side and here comes to lie in its normal position as the iliac and pelvic colon. In addition to the anomalies of rotation already described, we should mention the attachment of the cecum high up on the right, producing obstruction to the duodenum. This condition is handled by dividing the adhesions and permitting the cecum to assume a left-sided position. We have also seen that in volvulus in the small bowel, after the volvulus is untwisted there still remains a broad band or sheath from the cecum to the right wall of the abdomen, obstructing the duodenum. This is treated in a similar manner.

Last, a condition known as mobile cecum occurs in which there is not a normal posterior attachment. Such individuals not infrequently have a mesentery which is common to both small and large intestines. The cecum may be attached high on the right end of the liver or it may be unattached or the mesentery may be short and drawn over to the left side

with adhesions on the right. The diagnosis of a mobile cecum may be difficult. Patients complain of vague abdominal symptoms with intermittent bouts of obstruction. On exploration, mobile cecum with a normal oblique attachment of the mesentery can be tacked down posteriorly with suitably placed sutures. If, in addition, the mesentery does not have a normal posterior attachment, then it is probably better to slit the peritoneum at the right of the hepatic flexure so that the entire right half of the colon shifts over into the left side of the abdomen. This principle of mobilizing the colon so that it comes to lie on the left side, its primitive embryological position after re-entering the coelomic cavity, is one which is frequently utilized in colonic abnormalities with abnormal attachments. Volvulus of the ileocecal region and of the sigmoid have been discussed under the heading of intestinal obstruction. These are made possible by the unduly long mesocolon or mesocecum.

Congenital Megacolon or Hirschsprung's Disease or Idiopathic Dilatation of the Colon

The condition known as *megacolon* was described by Hirschsprung in 1886. It is generally believed that the cause of the greatly enlarged colon is due to a nervous imbalance. This is difficult to prove, and at times seems to be reputed by the various types of megacolon which may be limited to certain sections of the bowel. The parasympathetic nerves stimulate, whereas the sympathetics inhibit peristalsis of the colon. Also, the parasympathetics are said to relax the internal anal sphincter, whereas the sympathetics cause its contraction. To state this more simply, the stimulation of the parasympathetics increases bowel tone and causes relaxation of the sphincters, whereas stimulation of the sympathetics inhibits intestinal activity and causes a contraction of the sphincter. This is known as reciprocal or contrary innervation, and the external sphincter is under voluntary control. Thus an overactive sympathetic innervation or underactive parasympathetic may contribute to the development of megacolon. This undoubtedly is a factor in the causation of congenital megacolon. However, it cannot be the only factor because very often only small segments of the intestine are involved. There are probably various causes for megacolon. Reduced sensitivity of the bowel has been given as a cause; that is, in addition to the alterations of peristalsis of the colon and the tone of the sphincter muscle, there is a reduced sensitivity of the bowel so that the patient apparently does not know or does not receive the stimulus to empty the bowel, and because of this he will go for many days without defecating. There is, in addition, a great diminution of peristaltic movements and this, combined with the fact that there is no desire to defecate, accounts for the enormous dilation of the large intestine. The types of megacolon which are accompanied by some forms of obstruction due to congenital anomalies have been called *pseudomegacolon*. We have encountered these types more commonly than the usually described

general enlargement or uniform involvement of the large bowel which extends from the ileocecal valve down to the rectum. It has been our experience that the majority of these cases have an involvement down to the iliac colon or even lower, perhaps down to the superior valve of Houston. From here the enlargement is greatest immediately above this area and is diminished as the cecum is reached. This is exactly the reverse of the normal colon. There is a definite obstruction which can be demonstrated in such cases which accounts for this dilatation. There is a third group in which the dilatation is limited to one segment of the bowel. In such cases some type of obstruction can usually, although not invariably, be demonstrated. One last point which is important in the discussion of the etiology is the effect of drugs upon the megacolon. The response to atropine has been excellent in some cases. This is undoubtedly the type of case in which the function of the bowel is deranged due to nervous imbalance.

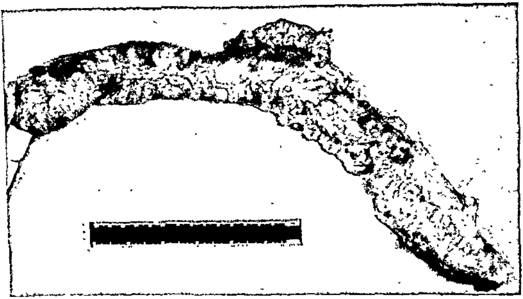

Fig. 302.—Hirschsprung's disease or megacolon. Photograph of gross specimen removed from R. B., a boy, 5 years of age, with Hirschsprung's disease. The operation consisted of a total colectomy with an anastomosis between the ileum and the pelvic colon at its lowest point. The boy had been in and out of hospitals since he was 2 years of age, with attacks of what was diagnosed as intestinal obstruction. When he entered the hospital there were five intestinal fistulae on the abdomen. These resulted from five different attempts at colostomy and enterostomy to relieve obstruction. Although the obstruction was finally relieved by the fifth operation, it was made in the small intestine so high that extreme emaciation resulted and excoriation of the abdomen took place.

The operation was planned in stages. At the first stage the ileum was divided near the ileocecal valve and the distal end brought out through a stab wound in the right abdominal wall. At the same time the sigmoid at its lowest point was divided and the proximal end of this was brought out through a stab wound on the left side of the abdomen. The distal end of the sigmoid at its junction with the rectum was left open, the proximal portion of the divided ileum was closed and anastomosed to the rectum in the manner of a side-to-end anastomosis and the abdominal incision was closed. The result of this first stage operation was an ileoproctostomy; the entire colon was left in situ with both ends protruding through stab wounds in the manner of a horseshoe.

At the second operation, which was done approximately four weeks after the first, the entire colon was removed through an upper transverse incision. This child has been followed in the outpatient clinic for the past four years. There was diarrhea for approximately eight months. When last seen in February, 1949, the child was in excellent health and attending school regularly. This illustrates the more complicated types of megacolon. The simpler varieties are those which have not had previous surgery. We have performed total colectomy in several of these with excellent results.

However, it is difficult to explain why diminishing the function of the parasympathetics which tend to stimulate contraction should produce improvement, and yet this is the case. It is easier to understand why such drugs as physostigmine, Prostigmine, and Mecholyl bromide, which are parasympathetic stimulants, would produce good results. In the same group of drugs is Syntropan, an atropine-like drug which paralyzes the parasympathetics.

Recently Swenson and co-workers have demonstrated that the primary lesion is in the distal portion of the colon at the rectosigmoid juncture and also in the rectum. This portion of the large bowel appears to be normal grossly. It is nondilated, and its wall appears to be of normal thickness. However, it has been shown that there is an absence of normal propulsive waves in the rectum and rectosigmoid by studies with a balloon in the rectum attached to a long catheter. This portion of the colon also shows an absence of ganglion cells which may account for the lack of peristaltic waves. Based upon this concept, Swenson and co-workers have designed an operation for the removal of the rectosigmoid and the rectum preserving the sphincter, and they have reported good results.

Pathological Changes.—The colon becomes enormously enlarged, sometimes being six or seven inches in diameter. The wall of such a colon becomes thick and the haustrations completely lost. There is a hypertrophy of the muscular coat, whereas the mucosa shows ulceration. Sometimes there is sloughing, and we have encountered two cases in which the bowel perforated spontaneously, producing peritonitis. Rarely the terminal ileum may be involved as well as the colon, and sometimes a megaloureter accompanies the condition.

The symptoms and signs of the condition are, (1) the greatly enlarged abdomen and (2) obstinate constipation. Children are known to go for days and even weeks without a bowel movement. In adults the same condition prevails, although the symptoms are not as marked. Diarrhea occasionally occurs due to the fact that there is a central fecal mass which permits only the liquid portion of the fecal current to go through. Late in the disease all the symptoms and signs of a chronic intestinal obstruction are present. There is great loss of weight, the abdomen is greatly distended, the diaphragm is elevated, there is atelectasis in the base of the lungs, the patient will not eat, and occasionally will begin to vomit, particularly those who have an incompetent ileocecal valve. Rectal examination shows, as a rule, the sphincter to be relaxed and the entire colon to be filled with fecal matter. In fact, the impaction is so great that the fecal matter must be removed manually. Barium enema with x-ray examination will show the enormously dilated colon. Postevacuation film shows an inability of the colon to empty itself. As a rule, the flat plate of the abdomen by the x-ray will give sufficient information to make the diag-

nosis. The reason for barium is that at times it may reveal the site of the obstruction in the particular type of megacolon.

Treatment.—Treatment of megacolon depends upon the stage that it is in. In all cases the treatment should be begun early in life. As soon as the diagnosis is made, the mother is instructed in the care of the bowel function of the child. A careful regimen of bowel habit, including a low residue diet together with a suitable cleansing agent such as physiological saline by enema, is useful. Occasionally when an impaction occurs the bowel must be cleansed by manual extraction. Drug therapy is helpful. The first group of drugs include parasympathetic stimulants such as Prostigmine, acetyl beta methylcholine (Mecholyl chloride), acetyl beta methylcholine bromide (Mecholyl bromide), tetra ethyl ammonium bromide, and Priscoline. These drugs have been used with a varying degree of success. In our experience, however, they have not been very beneficial over a long period of time. Prostigmine is useful and occasionally helps. However, here again, after the drug has been used for a while, the bowel ceases to respond as it does when it is first employed. The second group of drugs are the atropine group, of which atropine itself is perhaps as good as any, although we have had fairly good success with Syntropan. Most of these cases of the particularly obstinate type ultimately demand some type of surgical intervention, although patients with minor degrees of this condition go through life without help but with a good deal of bowel difficulty. This is proved by the fact that so many times we are astounded to find in older individuals who have had x-ray examinations with the barium enema enormous dilations of the large intestine and yet they live in comparative comfort.

Among the surgical procedures which have been recommended are (1) cecostomy to relieve the distress and to serve as a life-saving procedure in cases of obstruction; (2) resection of the dilated loop or complete colectomy; (3) removal of a portion of the sympathetic nervous system. Of the three, the removal of a portion of the sympathetic has been favored by many observers. Before this is attempted, it is well to perform a therapeutic test by inducing a spinal anesthesia. With anesthesia as high as the nipple, flatus and feces are passed per rectum if the overactive sympathetic is at fault. Sometimes after the use of spinal anesthesia there will be several large bowel evacuations during the following twenty-four hour period. A barium enema may be given, after which a spinal anesthetic or acetylcholine bromide should be injected. Twenty-five minutes later a film is taken and the effectiveness of these drugs may be determined. It has been generally believed that if the bowel does not empty after the injection of spinal anesthesia the tone is gone and the changes are irreversible and lumbar sympathectomy will not help, whereas if it is successful in emptying the bowel, sympathectomy will be useful. The abdominal sympathetic chain has an outlet through the first, second, third, fourth, and fifth lumbar ganglia which lie on either side of the great abdominal vessels.

Fibers pass medially from each ganglion to form a plexus over the aorta. This is continued down over the promontory of the sacrum and is known in this region as the hypogastric or presacral plexus which gives off fibers to supply the rectum, pelvic viscera, and genitals. The lumbar chain may be removed or the presacral plexus and its branches may be excised. This is an easier operation than lumbar sympathectomy perhaps, but it may interfere with the ejaculatory apparatus and produce sterility, while in the female it may interfere with sexual orgasm. The lumbar sympathectomy does not permanently alter the function of the bladder or the reproductive system provided the first ganglion is not disturbed. It does, however, produce vasodilation in the leg on the operated side. Most surgeons recommend the transperitoneal approach. This, of course, is safe and gives the surgeon the opportunity of studying the condition of the bowel. The mesosigmoid is incised, and the colon is rotated medially until the sympathetic plexus is encountered, and here the second, third, fourth, and possibly the fifth ganglia can be excised. The operation may be done on the right side in a similar manner to that on the left if the entire bowel is involved. It is perhaps well to do this in one stage. We have performed lumbar sympathectomy extraperitoneally through a transverse incision just above the umbilicus. The first lumbar usually lies under the renal and the fourth under the common iliac vessels. This is described in Chapter 6 in connection with the treatment of Berger's disease. This extraperitoneal operation is much simpler and in most instances can be accomplished with little difficulty, particularly in the adult. In the child it is perhaps better to explore and carry out the operation transperitoneally. Our experience with the operation has not been as good as has been reported by some observers. Several of our patients have returned after ganglionectomy with recurrence of the condition, although it must be admitted that they did receive temporary relief. Some have advised that in addition to excision of the ganglia that there should be carried out at the same time an excision of the hypogastric plexus and its branches. The operation of sympathectomy should not be done in children under 3 years of age, because a more conservative management should be tried until the child is at least 3 or 4 years old. The operation of cecostomy or appendicocecostomy is usually done because of an acute intestinal obstruction. It is a temporary procedure and is of very little value because the cecostomy, as a rule, does not function. It should be remembered also in the performance of a cecostomy that the sigmoid, being large and tending to be on the right side in the young child anyhow, is apt to be mistaken for the cecum in doing a cecostomy. We have seen two patients who have been referred to the Riley Hospital in which the treatment was recorded as cecostomy but at operation it was found that in reality there had been a sigmoidostomy. Any type of drainage is to be regarded as a temporary measure and not in any way curative. The treatment of megacolon before irreversible changes have occurred in the wall of the large bowel may be that recommended by Swenson and co-workers; namely, the re-

section of the rectosigmoid with preservation of the sphincters. In this type case, however, we have felt that perhaps a simple procedure may be used; namely, the division of the normal-appearing bowel by a longitudinal incision and then suturing it transversely very much like a Heineke-Mikulicz pyloroplasty. Although this does not remove the nonpropulsive segment, it does provide ample space for drainage and at least in one portion of the circumference enables the peristaltic waves to follow through. In particularly obstinate types of megacolon which fail to respond to the ordinary medical regimen or to sympathectomy, colectomy is indicated. In fact, we have come to employ this method more frequently now than formerly after making sure of the type of megacolon that is present. This attitude has come about due to the effectiveness of the sulfonamides, such as Sulfasuxidine and Sulfathalidine, which are useful in reducing the flora of coliform organisms in the large intestine. Resection may be done in one stage which is not so difficult in the young child, or if the case is complicated and has had previous surgery, it may be done in two stages. The first may be an anastomosis between the ileum and the lower sigmoid, bringing out the distal end of the ileum as a marker and also to prevent any inside leakage from the inverted distal end; then at a second stage the bowel may be removed. We have one child in whom we performed the first stage and brought out the distal end of the ileum as well as the proximal end of the sigmoid, after performing an anastomosis between the proximal ileum and the lower sigmoid. This horseshoe of small and large bowel which remained was later successfully removed (see Fig. 301). It has been interesting to note that the child has improved greatly, has grown normally, and has absolutely no symptoms. Further observations concerning medical management of megacolon has led us to favor radical surgery because mortality rates varying from 19 to 79 per cent and averaging 58 per cent appear in the literature when medical management is the treatment that is persisted in. The results from sympathectomy are much better. The mortality for this operation is low, and great improvement ensues in a large number of patients. Although the mortality of colectomy was formerly forbidding, under present treatment, preoperative preparations, and postoperative care, the mortality has been reduced to a degree which has brought about its use more frequently.

Last, the treatment of associated conditions must be considered. Since the condition may result from organic obstruction of congenital origin, it is, of course, obvious that if there is a congenital stenosis of the rectum or anus, this must be corrected. Also in the cases of redundancy of the colon or the so-called dolichocolon, which are notoriously apt not to be benefited by sympathectomy, colectomy is probably the treatment of choice. Other factors such as hyperthyroidism, avitaminosis, and malnutrition should be corrected whether the surgery is performed or not. Acetyl beta methylcholine bromide is given in doses of 1/10 Gm., increased if necessary to 2/10 Gm. within two to three days. Then after several more days

with this daily dose, 1/10 to 2/10 Gm. in mid-afternoon may be prescribed in addition to the morning dose; later, 2/10 Gm. given each morning and in mid-afternoon. The abdominal sympathectomy is perhaps best done transperitoneally because it gives the surgeon an opportunity to examine the entire colon. Both sides may be done at the same time. However, it should be stated that sympathectomy does not always immediately restore the involved bowel to normal functional activities. In one last point, in colectomy, due to the poor healing quality of the distended bowel, every effort should be made to keep the bowel clean for a period of two weeks before surgery and sulfasuxidine is administered. The anastomosis should be low and into as healthy bowel as possible and should be of the lateral type rather than the end-to-side or the end-to-end variety. However, in the last patient that we operated upon, this was not feasible and a side-to-end anastomosis between the terminal ileum and the lower sigmoid was successful.

Congenital or Familial Polyposis of the Colon

Although many types of polypi may occur within the alimentary tract, we are especially interested here in multiple polyps which occur chiefly in the large bowel in children. This has been called congenital polyposis of the colon rather than hereditary polyposis because babies are not born with the disease (see Chapter 10). Later in the chapter we shall consider other types of polypi; however, this discussion is limited to the congenital types. The etiology is obscure. However, it is thought that it is a congenital error of the development of the epithelium itself. Since the disease does not occur at birth but develops later in life, it is perhaps better to use the term congenital rather than hereditary polyposis. Perhaps the forerunner or the soil in which the polypi develop is hereditary. The hereditary aspect of the disease has been studied by many observers, most of whom believe that it occurs in mutations of the genes of the individual who has not exhibited the disease and he passes the mutated genes on to his children. These may be passed on as a dominant or recessive. If dominant, the disease occurs in every generation; if recessive, both parents must carry the mutated genes before the condition may be seen. Many observers believe that in multiple polyposis the gene is a mendelian dominant. It is certain that whenever the disease is found in any individual all members of the family should be examined and should be subjected to repeated examinations at least at six-month intervals because the disease does not necessarily appear before puberty. Multiple polyposis may occur as a result of chronic irritation or infection, and in chronic ulcerative colitis there is a tendency toward polyposis due to the fact that there is a destruction of areas of mucous membrane interspersed with areas which are not completely destroyed, giving a polypoid appearance. The polypi in this disease vary in size from 1 mm. to 2 or 3 cm., and they may be pedunculated or sessile. We have seen patients in whom the polypi were so numerous that there was hardly an area of normal mucous mem-

brane between them. A further interesting observation concerning the pathology relates to the tendency toward malignancy. The tendency is so great that some observers believe that all patients who have congenital polyposis ultimately will develop malignancy in some of the polypi if they live long enough. Perhaps nowhere else can change from normal mucosa to inflammation, gland cell hypertrophy, adenoma, and adenocarcinoma be so clearly demonstrated as in multiple polyposis of the colon.

The *symptoms* and *signs* of this disease vary, but chiefly there is bleeding. When the polyp is high up, the blood may be darker in color and when low down it may be bright. If there is a very small amount of bleeding, the occult blood in the stool would be demonstrable only by chemical tests. By far the more frequent cause of bleeding comes from

Fig. 303.—Congenital polyposis of the colon. This patient was a young woman, 29 years of age, who came to the hospital because of bleeding from the rectum. The onset of the symptoms occurred two years prior to her admission. However, there had been times, even in childhood, when the patient's family reported that she had had bloody stools. Her family history is interesting because her father and a sister died of cancer of the rectum at the respective ages of 41 and 26 years. Both paternal grandparents died of cancer of the rectum. The sigmoidoscope showed multiple polypi, some of which were ulcerating and bleeding. The barium enema demonstrated numerous polypi in the entire ascending colon and left half of the transverse colon. The photograph is a close-up of the gross specimen removed by radical resection of the entire colon. No areas of carcinoma were found in the polypi. Because of the patient's history and the family history and extensiveness of the polypi, radical resection was indicated and was carried out The incidence of carcinoma in congenital polyposis of the colon is so great that even though there is no proved carcinomatous degeneration, total colectomy should be done.

polyposis of the lower colon. Sometimes there is abdominal pain, or there may be a prolapse of the anus. If the polyps are low enough, they may be felt by digital examination. The abdominal discomfort and pain may resemble that of an intussusception, and indeed sometimes the diagnosis between the two is difficult. Rarely there may be symptoms of nausea, indigestion, fatigue, loss of weight, and loss of appetite. The diagnosis is made by the proctoscope and by a barium enema examination by the x-ray. Fortunately those polyps which cannot be demonstrated by barium enema

are usually present in the lower portion of the sigmoid and in the rectum. These, however, can be demonstrated by proctoscopic and sigmoidoscopic examination. Since congenital polyposis may be accompanied by polypi in the small intestine as well as in the stomach, it is also our custom to do a complete gastrointestinal examination with the barium meal in the hope that by repeated x-ray examinations, as the meal courses through the bowel, polypi will not be overlooked high in the alimentary canal. The differential diagnosis is as follows: Bleeding from the rectum in a child is usually not serious and implies a gastroenteritis. Sometimes there is constipation, and rectal bleeding will occur from that. There may be an anal fissure which will break open and cause some bleeding. Other conditions which cause bleeding are Meckel's diverticulum, intussusception, scurvy, and blood dyscrasias. These have been discussed previously in this chapter, however, routine hemoglobin red blood and platelet count, clotting and bleeding time, together with red blood cell fragility tests, may be necessary to rule out systemic causes for the bleeding.

The *treatment* of multiple polyposis of the colon depends upon the extent of the disease and the portion of the bowel involved. With a limited number of polypi, abdominal exploration may be done with ileotomy or colotomy and the polyps excised with a cautery. With modern methods of preparation with Sulfasuxidine or Sulfathalidine, the large bowel may be opened at various sites, the polypi removed, and then the colon may be closed safely without fear of peritonitis provided that a careful technique is followed. The treatment of choice, however, is colectomy followed by an ileosigmoidostomy. This is true because one cannot be sure even using the utmost of care that all polyps have been removed, and, furthermore, since the colon has a fertile soil for future development of polypi, we have found that in those patients in whom we thought we had removed all visible and palpable polypi new polypi occurred at the sites which had not been previously involved. Since the lower six or eight inches of the bowel also contain polyps, these are removed through the proctoscope; then an ileosigmoidostomy and a colectomy are performed. We have recently done this as a two-stage operation. The first stage consisted of destroying the polyps with the sigmoidoscope and the second stage consisted of a colectomy with an ileosigmoidostomy. Ladd has recently reversed this procedure, using the following technique in a child who was bleeding profusely from many polypi in the colon. The first stage consisted of transection of the lower ileum, establishment of an ileostomy, resection of the terminal ileum, cecum, and entire colon down to the lower sigmoid, and turning in of the lower sigmoid to make a blind rectal pouch about six inches long. In the second stage the polyps were removed through the proctoscope. In the third stage the ileostomy was taken down and an ileosigmoidostomy was performed. The number of stages required would obviously depend on the condition of the patient. If the patient is in a desperate condition, it is always better to perform the operation in stages;

however, if the patient can be properly prepared, colectomy and anastomosis between the ileum and the lower sigmoid may be safely performed in one stage.

Hereditary Hemorrhagic Telangiectasia

One last congenital defect which produces bleeding from the gastrointestinal tract must be mentioned for completeness. It is extremely rare and is known as *hereditary hemorrhagic telangiectasia.* It is an inherited dominant characteristic. The sexes are equally affected and either sex may transmit it. Sometimes epistaxis beginning in childhood is the first manifestation. Hemorrhages are not limited to the large bowel and may occur anywhere, including the mucous membranes and skin. The diagnosis rests upon the visible demonstration of telangiectases which is often difficult without exploratory operation. The basic pathology is a thinning of the vessels, particularly of the muscular coat. This results in a bulging of the wall and a defect which may be extensive. The lesions are noted most commonly in the stomach and the sigmoid colon. The treatment of the lesion has been unsatisfactory, although remedies for the anemia, such as iron and repeated transfusions, are indicated; also vitamins C and P have been used with equivocal results.

Hemangioma

Another condition which appears extremely rarely and which may be classed as a congenital anomaly is the presence of a tremendous type of hemangioma. We have encountered one case in which the lowest sigmoidal artery spread out and formed a tremendous hemangioma. This bulged into the sigmoid and produced bleeding. The vessels were tied off and resection with anastomosis was done. The patient recovered and has had no recurrence of bleeding.

Spastic Colon

The *colon*, like the stomach, is subject to nervous disorders, which may cause *spasm* (spastic or irritable colon), or great *dilatation* (because of spasm at the sphincter), or *atonicity*. In fact, *megacolon* of minor degree is said to be due to overaction of the sympathetic nerves (which constrict the sphincters and decrease peristalsis). The x-ray reveals the spastic colon as a contracted tube and the colon of megacolon as a widely dilated one. The treatment of spastic colon consists of dietary management and sedation and the use of atropine or atropine-like drugs. Megacolon is treated by dilation of the rectal sphincter, repeated colonic irrigations, and a low residue diet. Sometimes sympathetic ganglionectomy is done. If all other methods fail, *colectomy* is indicated.

Diverticulitis of the Colon

The word diverticulum means, literally, a by-path. It is a blind tube, or sac, branching off from a principal channel. We may look upon four

classes of diverticula: (1) a normal functioning pouch for storage and absorptive purposes, such as the gall bladder, or (2) those natural pouches whose function is unknown, such as the appendix; (3) a congenital defect, or so-called "true diverticulum," containing all the layers of the wall of the organ involved, such as Meckel's diverticulum, or other congenital diverticula of the small or large bowel; (4) acquired, or so-called "false diverticula," such as esophageal, urinary bladder, and colonic diverticula.

Sometimes diverticula occur as a compensatory mechanism, not only to relieve pressure but to increase retention space or provide more area for absorption of fluid. An example of this is the dilatation of the bile ducts, with the formation of parietal sacculi after extirpation of the gall bladder.

Incidence.—A study of diverticulosis of the large bowel and its complications is timely because of its commonness. An accurate survey of world statistics, including the twenty-three cases we are reporting, has led to the following conclusions: (1) the disease is practically always acquired; (2) it is rarely encountered in persons under 30 years of age, where the incidence is about 0.5 per cent; (3) over 40 years the incidence in the general population is variously estimated at 5 to 10 per cent and is more common in males, 1¼ to 1; (4) complications develop in about 15 to 25

TABLE XVII

CLINICAL TYPES OF DIVERTICULOSIS

TYPE		NUMBER OF CASES
I	Diverticulosis without symptoms	2
II	Diverticulitis with vague abdominal pain and bowel dysfunction (constipation and diarrhea or both)	6
III	Diverticulitis with symptoms and signs of appendicitis	2
IV	Diverticulitis with symptoms and signs of large bowel obstruction and the presence of an abdominal tumor	5
V	Diverticulitis resembling left-sided appendicitis, with perforation and general peritonitis	1
VI	Diverticulitis with urinary bladder symptoms	2
VII	Diverticulitis with external fistulae	1
VIII	Diverticulitis with colonic bleeding	3
IX	Diverticulitis associated with ulcerative colitis	1

TABLE XVIII

COMPLICATIONS OF DIVERTICULOSIS

I. Acute diverticulitis
  A. Gangrene with perforation
    1. Spreading peritonitis
    2. Localized abscess
      a. Secondary abscess by continuity
      b. Pylephlebitis with multiple liver abscess
      c. Subphrenic or perinephric abscess
      d. Empyema
    3. Rupture into bladder, bowel, or other viscera, or to exterior
II. Chronic diverticulitis
  A. Colitis
    1. Hemorrhage and ulceration
  B. Pericolitis
    1. Obstruction
    2. Adhesions to other viscera

per cent of this group; and (5) from 25 per cent to 50 per cent of these complications demand surgical intervention for relief. In other words, 3 to 5 per cent of all cases of diverticulosis demand surgery, and these complications are more common in females, 2¾ to 1. Thirteen cases in our group, or 56.5 per cent, were treated medically; surgery was necessary in seven, or 30.4 per cent, whereas three were not treated. (Tables XVII, XVIII, XIX, XX.)

Table XIX

Age Distribution in Diverticulosis

20 to 30	3
30 to 40	2
40 to 50	2
50 to 60	6
60 to 70	5
Over 70	4

Table XX

Location of Diverticula in Twenty-Three Cases of Diverticulosis of the Colon

LOCATION	NUMBER	%
Sigmoid (sigmoid includes iliac and pelvic colon) colon	8	34.7
Descending and sigmoid colon	6	26.0
Transverse and descending colon	3	13.0
Transverse, descending, and sigmoid colon	3	13.0
Transverse colon	1	4.3
Ascending colon	2	8.6

Etiological Factors.—Although the exact etiology of diverticulosis is unknown, *many factors are known to contribute to its occurrence.* These may be grouped as follows: (1) embryological, (2) anatomical, (3) physiological, (4) pathological, (5) physical (Table XXI).

A careful review of the evidence concerning the cause of this disease reveals the following facts:

1. Diverticula are usually acquired, and are seen frequently in people past 40 who are more often of the lateral than the linear types, although they must be thought of in all ages and types.

2. They are usually found in the pelvic and iliac colons but may occur throughout the large bowel.

3. They may be present anywhere on the circumference of the bowel, but are usually found (a) along the anterior taenia and (b) on the mesenteric side of the anterior and posterolateral taenia, where vessels penetrate the wall of the colon.

4. The cause of diverticulosis is probably a combination of factors due principally to an increase of intraluminal pressure and a decrease in the resistance of the intestine's wall to this pressure. The former may be influenced by (a) the smallness of the bowel lumen at the junction of the rectum and sigmoid, (b) constipation (although *this is doubtful*), (c) spasm of circular muscle, and (d) obesity, causing increased intra-abdominal pressure (although diverticula also are found in thin persons).

The latter, that is, the decreased resistance of the bowel wall, may be influenced by (a) large canals for the entrance and exit of vessels, (b) congenital defects, and (c) wear and tear of muscle as age is increased.

5. The foregoing factors are all present in the pelvic colon, where there is a small space in a transverse position which bears the brunt of

TABLE XXI

ETIOLOGICAL FACTORS IN DIVERTICULOSIS

I. *Embryological Factors*

1. Congenital anomalies are rarely found in hind-gut except at its terminal portion, which may be blind, or in rectum. The anus is a common site.

2. Many congenital (true diverticula) may occur as determined by the presence of all layers of the colon; however, these layers may become thinned or separated later in life, leaving only the mucosa and submucous coat.

3. Congenital anomalies usually are not so multiple in an organ, although they may be in various organs coincidentally.

4. The incidence increases with age.

5. At birth, only the terminal part of the pelvic colon lies in the pelvis.

6. The bowel in its development grows away from the vessels, tending to produce traction upon its walls.

II. *Anatomical Factors*

1. The colon is wider at the cecum (3 inches) and narrower at the sigmoid (1½ inches or less).

2. The pelvic colon lies in a horizontal plane, giving rise to stasis.

3. The longitudinal muscles only partially cover the large bowel by three longitudinal bands known as "taeniae." Even in its lowermost portion these muscles do not completely encircle the bowel.

4. The taeniae are one-sixth shorter than the bowel, giving rise to sacculations These form three rows and are definitely divided by the well-developed circular muscle. The sacculations, when distended, resemble large diverticula.

5. The appendices epiploicae along the anterior longitudinal band offer a site of least resistance.

6. The blood vessels create a real defect in the circular muscle layer and according to Edwards, are the points of least resistance.

7. Passive congestion in the veins, which are normally larger than the arteries, or lymph vessels seem to play an important role.

III. *Physiological Factors*

1. There is little peristalsis in the colon except for the powerful rush waves which fill the pelvic colon from below upward.

2. The Sigmoid is the most sensitive portion of the large bowel, giving rise to spasm here. When fully distended, the sacculi bulge outward, providing more space for storage.

IV. *Pathological Factors*

1. Spasm of circular muscles.

2. Adhesions cause traction diverticula.

3. Muscle deficiency on either side of the anterior taeniae which leads to herniations into the appendices epiploicae. This deficiency is due to:

   a. Wear and tear of age.

   b. Muscle degeneration

   c. Increased pressure within, due to constipation or other causes.

4. Muscle atrophy sometimes occurs.

V. *Physical Factors*

1. Diverticula can only occur as a result of two forces:

   a. Increased pressure from within; that is, pulsion.

   b. Pulling from without, that is, traction.

   These factors are effective when there are local points of lowered resistance.

2. Experiments in cadavers, in which an increase in intraluminal pressure was produced, caused a rupture of the bowel at the mesenteric border. In living persons, air injected under high pressure into the rectum may cause a perforation in the antimesenteric border. In living dogs, such pressures also cause a break in the antimesenteric border.

3. Sudden increase in intraluminal pressure following obstruction resections or the injection of large amounts of water for enema may cause perforation at various points on the circumference of the bowel.

high intraluminal pressure because of the weight of the fecal content; the rush peristaltic wave with filling from below upward and the squeezing action on the outside tend to force pouch formation if any weakness exists in this area. This probably accounts for the fact that about 86 per cent of all diverticula of the large bowel are found here. (Tables XX and XXI.)

Pathology.—Diverticula may be covered with mucosa and submucosa only, or with fibrous tissue and a few longitudinal muscle fibers, subserous fat and serosa, or variations of these layers, but hardly ever by circular muscle. Diverticula may be microscopic in size and thereby evade detection by x-ray or gross inspection, yet give rise to symptoms and signs.

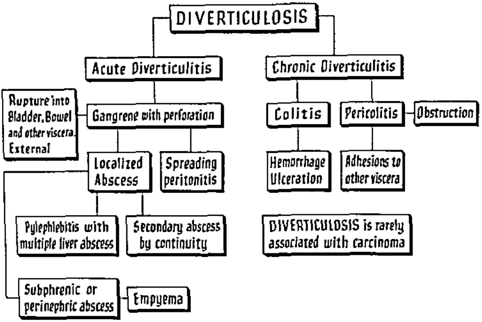

Fig. 304.—Chart indicating complications which may ensue from diverticulosis of the colon.

We are here more interested in complications of the diverticula. These may be simple inflammation, which may be severe enough to interfere with the blood supply, causing gangrene with perforation. This complication may in turn give rise to (1) local abscess formation, (b) general peritonitis, and (3) fistula. In addition, the diverticula may become chronically inflamed, causing a thickening of the entire bowel wall or sigmoiditis with or without pericolitis with fibrosis (gas pipe colon). Last, as a result of either the acute or chronic processes, obstruction of the lumen of the bowel may occur with all of the pathological changes and effects of intestinal obstruction. (Table XVIII.)

We must also mention the complications of acute inflammations in the abdomen, such as pylephlebitis with liver abscess, subphrenic abscess, and empyema, or even septicemia, and in all instances the enormous area

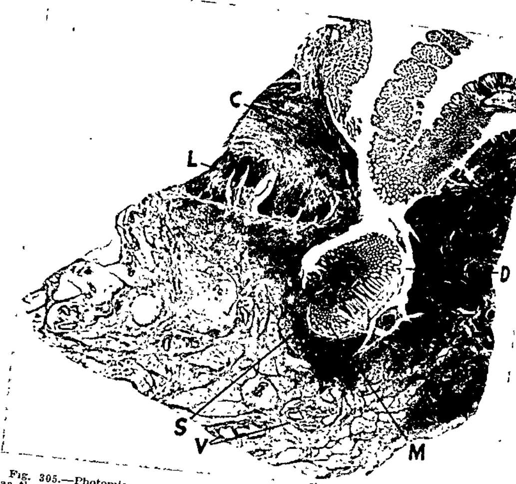

Fig. 305.—Photomicrograph of a small diverticulum from a resected sigmoid which was the seat of a chronic diverticulitis with obstruction. *C*, Circular muscle; *L*, longitudinal muscle; *D*, diverticulum; *M*, mucous membrane; *S*, submucous coat; *V*, blood vessel. (From Berman and Bauer: J. Indiana M. A. 35: 197, 1942.)

Fig. 306.—Diverticulosis of the colon, with stricture due to adenocarcinoma. The patient was a man aged 74 years. Arrow 1 points to a diverticulum, and arrow 2 points to the site of constriction due to adenocarcinoma.

involved in widespread inflammation gives rise to hemoconcentration and stagnant anoxia, which may be more important in the causation of severe systemic effects than the infection.

Symptoms and Signs.—Uncomplicated diverticulosis causes few, if any, symptoms or signs, and its diagnosis depends entirely upon the barium or double contrast enema. The complications present signs readily interpreted in most cases; however, almost any lesion of the large bowel may be mimicked. There may be sudden pain which begins and remains *in the left lower quadrant, together with* little nausea or vomiting, but with great tenderness and rigidity, with or without demonstrable air beneath the diaphragm on x-ray, indicating a perforation. This must be

Fig. 307.—*A*. Diverticulosis of the descending colon. Arrows point to the diverticula. *B*. Polyposis of the colon. Arrows point to some of the polypi. The patient was a young woman aged 28 years whose mother also had malignant degeneration from polypi of the colon. At operation the entire colon was found to be filled with polypi. Radical resection was done.

contrasted with the chronic case which presents symptoms of bowel dysfunction not unlike carcinoma, with alternating constipation and diarrhea. Last, the classical finding of gas and foul urine through the urethra is diagnostic of vesicocolic fistula. The relatively low temperatures (that is, without pylephlebitis or liver abscess) and low counts are interpreted as being due to the diffusion of the inflammation, which does not accumulate under pressure. This is not true when abscess or spreading peritonitis is present.

A word of caution is necessary concerning the presence of a mass, blood in the stools, and x-ray interpretations. All may point to a car-

cinoma, but all may, and often do, occur in diverticulitis. The pouches fill with granulation tissue which bleeds easily, and because of this, or swelling, or foreign bodies, they will not fill with barium, giving only the long ragged outline which, except for the length of the bowel involved, resembles carcinoma. One must always consider malignancy in these cases, because they occur in the proper age group, yet the incidence of this disease in diverticulitis is very low. One of our patients had a carcinoma of the prostate, another carcinoma of the colon, arising in polypi.

Prognosis.—The prognosis in diverticulitis, regardless of the mode of treatment, is not good. Hayden reports forty-four unoperated cases, of which three died in the hospital, fourteen died later, and twenty-seven are alive, with eight having recurrent attacks. Of forty-nine operated cases, twenty-eight died and twenty-one are living, five having recurrences. Of this latter group, thirty-one had only one operation, whereas eighteen had two or more operations. Arnheim reports an operative mortality of 62 per cent. Lockhardt-Mummery is less lugubrious in his outlook. Of one hundred and thirty-six cases, ninety-one were treated by operation and forty-five were not. The mortality was just over 10 per cent.

In the twenty cases treated in our series, seven were operated upon, with one death, the mortality rate being 14.2 per cent. In thirteen cases, no surgery was used and the mortality rate was 7.6 per cent (one death). The total mortality for the twenty cases was two deaths, or 10 per cent (Tables XXII and XXIII).

TABLE XXII

TREATMENT

Nonsurgical	13
Surgical	7
No treatment	3
Types of surgical treatment	
Resection of sigmoid	1
Inversion of diverticulum	3
Drainage of abscess	2
Cecostomy	1
Cecostomy—exteriorization of loop of sigmoid and later replacement	1
Closure of fistulae	1

Mr. O. K. had two operations—cecostomy and later drainage of abscess.
Mr. H. Y. had two operations—inversion of diverticulum and drainage of abscess.

TABLE XXIII

MORTALITY RATES

Nonsurgical	1 death in 13 cases
Surgical	1 death in 7 cases
Death from other causes	3
Diverticula an incidental finding	2 deaths in 20 cases
Total mortality rate	(10%)

Treatment.—Uncomplicated diverticulosis requires no treatment. Diurnal evacuations are desirable, and large enemas or cathartics may

be harmful. It is best to use agar or other bulk laxatives to keep the stool in one mass.

1. Acute diverticulitis should be treated with low residue diet, bed rest, sulfonamides, attention to water balance, and blood transfusions when anemia or hemoconcentration occurs. Unnecessary exploration should not be done because it is not innocuous.

2. Sudden perforation requires surgical intervention with turning in of the perforated diverticulum, if feasible, and then wrapping with omentum. If not feasible, the loop should be mobilized and placed outside the abdomen, and a tube anchored.

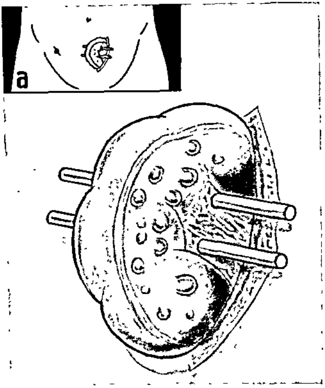

Fig. 308.—Loop colostomy.—Diagram illustrating a method of performing colostomy where a large loop of sigmoid is brought to the outside so that a complete exclusion may follow or in cases where the diseased loop is so large that a single bar will not permit the extrusion of the entire involved segment. The insert *a* shows the position of the colostomy. The same operation may be done by sewing skin beneath the colon as first described by Mixter. However, this necessitates dividing the mesocolon or mesosigmoid, interfering with blood supply and requiring a later open anastomosis. For a temporary colostomy, particularly in patients who are in poor condition and who will not stand much manipulation, it is, perhaps, best to bring a loop of sigmoid out and hold it out with a glass bar or a rigid rubber tube and loosely suture the bowel to the peritoneum. The bowel may be opened within twenty-four to forty-eight hours. If immediate decompression is required, a vent may be made by inserting a small catheter into the extruded loop and holding the catheter in position with a purse-string suture of silk.

3. Local abscess should be adequately drained through a muscle-splitting incision.

4. Spreading peritonitis is treated in the classical manner, with nothing by mouth, tube suction together with ample drainage, sulfonamides, blood and plasma transfusion, and intravenous medication.

5. Fistulae are treated by dividing the fistulous tract and turning in both sides, then interposing *omentum*. *In addition, some form of diversion* of fecal current may be temporarily necessary.

6. Chronic diverticulitis without obstruction is best treated by resection. *However, when we remember the forces active in the causation of* diverticula, we can readily see that in many instances there may be recurrence near the site of anastomosis. Mikulicz's operation is difficult because of the short, thick mesentery. End-to-size anastomosis is better.

7. Chronic diverticulitis with any degree of obstruction demands first a diversion of the fecal current. This is necessary to deflate the obstructed bowel. It also enables the surgeon to make further studies, so that carcinoma may not be overlooked. *The following* procedures may be used: (a) appendicocecostomy, (b) cecostomy, (c) ileostomy, (d) transversostomy, (e) colostomy.

Of these, "spur" transversostomy is the best except in acute obstruction. Here appendicocecostomy is the most feasible and is easily done.

8. If obstruction is present and the diverticula extend very low, *resection with anastomosis is done. It is best to drain after* this procedure through the cul-de-sac in the female, and posterior to the rectum beside the coccyx in the male.

9. Chronic complicated diverticulitis with "*gas pipe*" colon defies extirpation because of dense adhesions, and diversion of the fecal current is the only feasible procedure. For this reason recurrent diverticulitis should be looked upon as a serious progressive *disease* which should be treated by resection, especially in the segmental types.

Inflammations of the Colon

Inflammations of the colon are known as colitis. They are classified according to their position and extent as cecitis, sigmoiditis, or general colitis or according to their presumable cause. It is *the latter* classification which lends itself to clinical use. For practical purposes colitis may be divided into three big groups:

1. Nonspecific: (a) acute transient, (b) simple ulcer *of the* cecum or sigmoid, (c) chronic ulcerative colitis, (d) colitis of unknown origin, (e) regional colitis or segmental colitis.

2. Specific: (a) tuberculous, (b) lymphopathia *venereum*, (c) actinomycosis.

3. Allergic and psychosomatic.

From this classification it may be readily seen *that colitis* may have many and various causes. In this group we have not included bacillary dysentery which is caused by bacilli of Shiga and which is an acute, definite infection of the bowel. This belongs *in the* classification of specific types. Also, amebic dysentery belongs in the specific types. However, this is described in the chapter on Miscellaneous Infections, Chapter 7.

Fig. 309.—Chronic ulcerative colitis. *A*. Photograph of the abdominal incision on the twelfth postoperative day. The wound has healed by first intention. *B*. Portion of the excised descending colon. The entire bowel is involved. *C*. Ascending colon. Note the polypoid appearance of islands of mucosa which remain. N. F. was a woman, 36 years of age, who came to the hospital complaining of diarrhea with twenty-five to thirty stools a day consisting mostly of blood and mucus, loss of eighteen pounds in weight in six weeks, nervousness and vomiting, and a continual fever.

Operations were done in three stages. In the first stage an ileostomy was performed. This relieved the patient greatly but she continued to have fifteen to twenty stools a day which were mostly blood. The septic type of fever continued. The second stage consisted of resection of the cecum, and ascending, transverse, and a portion of the descending colon. At the third stage the descending colon, sigmoid, and rectum were removed. The operation was done in February, 1941. This patient has remained well. She is the mother of five children and is working in a department store as a clerk. The ileostomy functions well, and the stools are well formed. (Case referred by Dr. R. D. Rosenack.)

Acute transient colitis is caused by the paratyphoid bacilli or other forms of infection such as staphylococcus which produce a transient irritation of the bowel with all the symptoms and signs of colitis; namely, diarrhea, large watery stools, and perhaps a small amount of bleeding. In this group also belong amebic dysentery and bacillary dysentery which are more or less acute and are specific in origin. The disease is recognized by repeated cultures and smears from the stools, proctoscopic examination, and a barium enema. The latter is important because of the frequent association of the symptoms and signs enumerated under carcinoma of the bowel with superimposed infection.

The type in which the surgeon has a great interest is the so-called *nonspecific idiopathic ulcerative colitis*, also known as chronic ulcerative colitis.

In all types of *chronic ulcerative colitis* the soil may be made fertile by the psychosomatic background or may be made fertile experimentally by obstructing the lymphatic drainage of the bowel. It has been shown experimentally that the mucosa of the colon has a special tendency to ulcerate, after all lymphatic drainage has been blocked. By using sclerosing solutions, this method of producing a chronic type of ulcerative colitis may be utilized in studying the disease in the human being. It has been shown that organisms may be injected into the lymphatics without producing ulcerative colitis. Simple obstruction, however, of the lymphatics will set the stage for a colitis which in many ways resembles that of the chronic ulcerative form. When the lymphatics of the small bowel are blocked, a more generalized enteritis is produced rather than one of ulceration. These experiments are important only in that they emphasize the fact that local factors, no matter what they may be, which lower the resistance of the mucous membrane of the large bowel may be the start of a chronic ulcerative colitis.

This *group* of chronic ulcerative colitis includes many different varieties and causes of colitis. However, a common error is to group them all together and call them all chronic ulcerative colitis. In this group may be included *streptococcic ulcerative colitis* which is said to be a distinct entity. The disease is said to have more or less typical pathological manifestations. Principally the differentiation of this particular entity is in the fact that its lesions begin in the most distal segment of the rectum, just above the anal canal, and then there is a diffuse involvement of the bowel. Such patients frequently present themselves with a history of frequent rectal abscesses with fissures and fistulae and state that they have had many operations upon the rectum only to have recurrences. The disease spreads upward until the entire colon and even the lower part of the ileum become involved. The bowel becomes diffusely narrowed and haustral markings are erased; the barium enema with x-ray gives a more or less typical picture.

The clinical symptoms and signs of the disease may manifest themselves in one of two different ways. First, the onset may be sudden and

abrupt with diarrhea which is persistent; there may be many bloody stools during the day and excessive amounts of purulent rectal discharge; the patient complains of pain, has fever and leucocytosis and is profoundly ill. The second type is the one which has been referred to previously and the symptoms of which are chiefly those of the rectum. In this type the patient will complain of repeated rectal inflammation and infections with a diarrhea and purulent discharge. The diagnosis is made by careful proctoscopic examination and x-ray examination, and this particular type is usually grouped as one of the chronic ulcerative varieties. A second type

FIG. 310.—Ulcerative colitis. Barium-enema x-ray, showing the ragged filling of the mucosal outline in the transverse and descending colon due to ulceration.

of nonspecific chronic ulcerative colitis which belongs in this group is the so-called *ulcerative colitis of unknown origin*. This is the one which still retains the name nonspecific or idiopathic, and here the disease resembles that of streptococcic ulcerative colitis so closely that it is difficult to distinguish the two so that many observers do not believe that the streptococcic variety so-called is a definite clinical entity. A third form is the *regional ulcerative colitis*. This may appear anywhere in the bowel but seems to involve only a small segment. It has many of the characteristics of a

regional enteritis. The diagnosis of this condition is by the history, symptoms and signs, and proctoscopic examination. However, if the lesion is high in the colon, even the sigmoidoscope will not reach the site of the pathology; therefore, the barium enema provides the most reliable information. The remarkable pathological change in regional ulcerative or segmental ulcerative colitis is the fact that a segment of six to twelve inches is all that is found to be involved with an abrupt change to perfectly normal bowel distal and proximal to the lesion. The rectum is not involved in this condition.

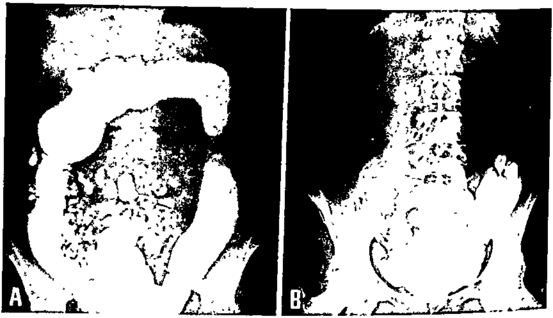

Fig. 311.—Regional colitis. A very unusual type of segmental nonspecific inflammation of the large bowel is regional colitis. *A.* Barium enema in a patient, Mrs. A. S., 42 years of age, who came to the hospital complaining of diarrhea, some blood in the stool, tenesmus, and cramping abdominal pain, with loss of weight of about twenty pounds within eight months. The x-ray photograph depicts the bizarre pattern of the large intestine. It will be noted that the cecum lies extremely high on the right side, and the appendix is visualized. Distal to the cecum are three knoblike projections from the smooth outline of the large intestine. Proctoscopic examination was normal.

At operation the entire ascending and transverse colon had shrunken and become fibrosed. What seemed to be a high cecum in the x-ray studies proved to be a contracted cecum and ascending colon. The cecum, ascending colon, splenic flexure, and descending colon down to the iliac colon was removed and the ileum was anastomosed to the iliac colon by side-to-side anastomosis. *B.* Postoperative barium meal study of the intestinal tract. The patient was last seen in February, 1949, three years after operation. She complained of occasional periods of loose stools, soon after operation. There was no loss of blood and no purulent discharge. Stools remained rather liquid. However, at the present time the stools have regained their normal consistency and the patient is now without symptoms. She has still failed to gain weight.

Lastly, another type of chronic ulcerative colitis which we placed in group three is the so-called *allergic* or *psychosomatic type*. There is evidence that ulcerative colitis may rest on a psychosomatic basis. The reason for this statement is that it seems to occur in a certain type person—the linear type, the introvert. Such individuals have frequently had bouts of regional enteritis and duodenal ulcer and then chronic ulcerative colitis. However, from a pathological and a roentgenological point of view the types which have been mentioned give pictures which are so similar that it

is difficult to state that they are each of them clinical entities. The different types of chronic ulcerative colitis have a fertile ground in certain type individuals, and whether or not the streptococcus or many bacilli and cocci are at fault depends entirely upon the flora which happens to be present in the greatest numbers. It is the "soil" rather than the "seed" which is the cause of the ulcerative colitis. Even in the regional types the entire bowel may ultimately be involved and frequently becomes diseased after resections and after anastomoses around the obstructed and inflamed areas.

In this chronic group belongs one other entity, *simple ulcer* of the *cecum* or the *sigmoid*. A single ulcer may appear either in the cecum or on the left side which spreads and ultimately may perforate. The entity has been seen more commonly on the right than on the left side, and moreover *an ulcer on the left side is usually a part or phase of chronic ulcerative* colitis. It cannot be denied, however, that simple ulcer of the cecum beginning on the mesial side near the ileocecal valve is a definite clinical entity. Its complications may include perforation or obstruction. Sometimes the entire cecum becomes involved and a resection may be required. chronic ulcerative colitis untreated is usually a progressive disease. However, it may undergo resolution and in the early types with proper management patients have been known to remain in a status quo or even to improve sufficiently to return to normal existence. We have seen women patients who have borne children without recurrence of the disease. However, the usual tendency is for the disease to involve all coats of the bowel. The mucosal surface is denuded to a greater or lesser extent, and although healing may occur here and there, there may be a heaping up of mucosal islands producing a pseudopolyposis, ultimately a stricture. The muscularis becomes thickened and the serosa is edematous, and although the bowel appears to be thicker, in reality it is extremely thin and friable. Healing of the muscular coat results in fibrosis and narrowing of the lumen, and frequently strictures occur.

Complications of the disease include perforation with general peritonitis or localized abscess, fistula formation, hemorrhage, stricture or narrowing of the lumen, pseudopolyposis, and malignant degeneration. The treatment of chronic ulcerative colitis includes medical management and surgery. There is a difference of opinion concerning the value of *ileostomy* in early cases of the disease. All are agreed that it should be done alone or as a complementary procedure in any of the above complications. Usually in the early phases of the disease, if there are remissions and exacerbations, in the periods of remission the patient believes that the condition has been arrested. The use of penicillin in large doses given in aluminum hydroxide gel and the use of Sulfasuxidine and Sulfathalidine may produce temporary remissions. Such patients are also given high vitamin, high protein diets with low residue, and on this regimen they may improve greatly. In addition, these patients frequently are

given neuropsychiatric care and this too seems to help. However, soon an emotional upset with acute infection occurs, and the process recurs with all its virulence. If the disease is allowed to progress and if the diarrhea is bloody, patients will develop severe anemia. Earlier, before the stools become bloody, there will be hemoconcentration due to loss of plasma in large amounts. This, in turn, is caused by frequent stools without blood. In either event, the blood volume is greatly reduced. Patients become extremely toxic. The formation of vitamin K_2 cannot take place because proper absorption does not occur, and very frequently there is a decided

Fig. 312.—Chronic ulcerative colitis in a child. Ileostomy performed in a case of chronic ulcerative colitis in a boy aged 14 years. There followed a great improvement of all symptoms and a gain in weight. The subsequent history of this child was as follows: Ileostomy was closed on two occasions but each time symptoms recurred. In addition, the lesion progressed until there was a constant bloody diarrhea so that the child deteriorated very rapidly. Because of this, a total colectomy was done in stages, with good results.

reduction in the prothrombin time. For this reason we have advocated the earlier use of an ileostomy if the patient fails to respond on a trial of medical management. The ileostomy can be disconnected and the continuity of the bowel may be restored if the patient becomes well. However, in most cases where ileostomy is employed the disease is in an irreversible form, and the ileostomy must remain. Therefore, when patients are getting

the benefit of an early ileostomy, there is a remote possibility that the bowel may be restored to normalcy. Our experience, however, has not borne out this fact. Perhaps it is due to the fact that we have not employed ileostomy early enough. However, even in a 16-year-old lad on whom ileostomy was done three times, the continuity of the bowel was restored, and each time the chronic ulcerative process recurred. The medical regimen included diet, psychogenic control, typhoid vaccine which has been advised by some, high vitamin intake, and the use of penicillin, streptomycin, aureomycin, Chloromycetin, and Sulfasuxidine. If the enterostomy proves effective in controlling symptoms, further surgery is not necessary. Vagotomy and lumbar sympathectomy may be used with ileostomy or as definitive measures. Their effectiveness remains to be proved in our hands. Ileostomy is done under local anesthesia through a McBurney incision. The ileum is divided and the proximal end is brought out through the incision in different planes of muscle so that sphincter action, which is primitive of course, may be attained. The distal end is brought out through a stab wound high up on the right side with a clamp on this end until the bowel wall has healed to the skin and to the peritoneum. The reason for this sort of procedure is that many of our cases have strictures in the lower rectum, and also many times the terminal ileum is not entirely free from the disease. Therefore, to turn in the distal end would be risky because of a chance for leakage. Furthermore, should colectomy be necessary, it will be unnecessary to dig up, so to speak, the turned-in distal end. Use of the transverse incision makes it possible to include the transplanted distal end in the incision, and in this way the ileum, cecum, ascending colon, and transverse colon may be removed at the second stage of the operation. In all cases in which ileostomy is unsuccessful in that the person still has chills and fever and still loses large quantities of blood as a result of diarrhea, it will be necessary to do a colectomy. This is done in two stages. The first includes removal of the terminal ileum and ascending colon, transverse colon, and the descending down to the upper sigmoid. The next stage includes the descending and the sigmoid and the rectum if necessary. In a few cases we have found that it is not necessary to do an abdominoperineal operation and that the distal end may be turned in. This is particularly true of the type which does not begin in the anus and the rectum. We have recently tried colectomy with preservation of the rectal sphincter and implantation of the ileum in the sphincter. The results were not as good as in abdominal ileostomy.

Of the *specific types of colitis,* tuberculous ulcerative colitis has been discussed in Chapter 8. It was shown in Chapter 8 that the tuberculous type of ulcerative colitis is primarily in the small intestine, although it sometimes may involve both small and large bowel. In the average case, tubuculous colitis is secondary to tuberculosis of the lungs or elsewhere in the body. Sometimes it is associated with tuberculous peritonitis with miliary tubercles on the serous surface of the bowel. Usually tuberculosis involves the ileocecal area, although the colon may be involved. Surgery

is indicated to relieve obstruction, and resection of the ileum and the cecum or the colon may be necessary.

Ulcerative colitis due to the virus of venereal lymphogranuloma has been described in Chapter 7. This usually results in a stricture, and the surgeon is frequently called upon to relieve the obstruction. There is no drug that has been successful in combating the disease, although emetine, streptomycin, the sulfonamides, penicillin, Frei antigen, estrogenic hormone, and other drugs have been used. Irradiation, diathermy, and solid carbon dioxide snow have also been employed with equivocal success.

Surgical methods include dilation with finger or bougies, internal proctotomy (division of the stricture within the rectum by means of an incision much like the operation of internal urethrotomy), complete or external proctotomy (incision through the stricture in the posterior midline through external posterior incision). Proctotomy gives only temporary relief and has not justified its use, although an occasional arrestment of the disease and alleviation of symptoms result. Permanent colostomy is the operative procedure of choice, although there are some objections to it. The disadvantages are: (1) the artificial anus, (2) stricture of the colostomy opening, (3) anterior herniation of the bowel, and (4) retrograde herniation. However, if the colostomy is properly performed, most of these objections are not valid. In addition to the permanent colostomy, an abdominal perineal resection may be indicated. Many other types of procedures have been advocated and all are variations of colostomy with or without excision. A word should be said concerning some of these. The two chief types are the so-called Pauchet's intrasphincteric excision operation and the large abdominal perineal resection. The Pauchet operation includes a preliminary colostomy and then a resection of the offending rectum, together with its stricture, from below and then suture of the proximal end of the upper sigmoid into the sphincter muscles. Later, at a third stage, the colostomy is closed. This operation can be used only in selected cases. It has in its favor the preservation of the sphincter and the closure of the colostomy. The operation can be used if the stricture does not extend too far upward; that is, if the stricture extends for more than six inches or about 15 cm. above the anus, the procedure cannot be used. It also cannot be used if the sigmoid is plastered down with adhesions within the abdominal cavity. However, there is much to be said for this procedure. Since the lesion is not a malignancy, if the sphincter can be preserved this is to be desired. If there is a failure, the patient is forewarned that colostomy may be necessary and the trial has been worth while. In extensive cases extending up into the peritoneal cavity with great and widespread adhesions or in those involving the entire rectum, the operation of abdominoperineal excision is best. Such cases defy the bringing down of the proximal loop, and to leave the disease in situ would mean to re-establish fistulae and sinuses.

Chronic bacillary dysentery follows the acute form and is due to one or several strains of *Shigella paradysenteriae.* The diagnosis depends upon

the presence in the blood of agglutinins in significant titer (at least 1 to 320 or higher) of one of the several strains of *Shigella paradysenteriae.* The treatment is based upon the use of the sulfonamides particularly succinylsulfathiazole and Sulfathalidine. In the more severe cases, and particularly those caused by the Flexner and Shiga strains of these organisms, specific serums and bacteriophages may be used, although these have not been of particular help.

Regional ulcerative colitis is difficult to diagnose even with the barium enema. This is due to the fact that there is extreme shortening and thickening of the bowel so that it resembles carcinoma, and differential diagnosis cannot be made without biopsy. In a recent case the entire ascending colon and cecum were pulled up, so to speak, into the transverse colon although not intussuscepted within the colon. The shortening of the ascending colon was so great that it appeared that the ileum entered a bulbous enlarged end of the transverse colon at the hepatic flexure. Resection and ileosigmoidostomy were done. It should be also stated that the disease tends to progress even after resection, which is the treatment of choice, and may recur very much as it does in regional enteritis.

Actinomycosis of the large intestine is found more commonly on the right than on the left side. It is said to originate in the appendix not infrequently. Diagnosis is rarely possible prior to operation. Even here the disease frequently is called a tuberculosis or malignancy. The biopsy proves the diagnosis. If the disease is localized to any segment of the bowel, resection should be done.

Sprue and *pellagra* may resemble ulcerative colitis of the idiopathic type. However, in most instances the appearance of the bowel through the sigmoidoscope will not show ulceration but rather a hyperemia. The x-ray examination shows dilatation of the large intestine with a minimal amount of change in the mucosal pattern. Also, these same changes are sometimes seen not only in avitaminosis but in certain *allergic types* of colitis. It has even been said that allergy may cause polyposis; that is, a piling up of the mucous membrane. Mucosal abrasions are seen through the proctoscope. However, there is no evidence that allergy causes a real severe form of ulcerative colitis. These conditions, as has been said previously, are amenable to dietary management, vitamins, iron, liver, calcium, and psychotherapy. Their importance lies in the fact that they provide the soil for virulent strains of bacteria to enter, causing the chronic ulcerative type of the disease.

One last entity which has been discussed in the literature at times has been the condition known as a *granuloma, nonspecific in type.* This is probably another form of so-called segmental or regional colitis and differs in no way that is apparent from the chronic ulcerative colitis previously described. In summary it may be stated that there are many diseases which are grouped under the heading of chronic ulcerative colitis. The

morbid process may vary in each of the different types, but in general there are gradual hyperemia and swelling and edema of the mucosa with or without small ulcers. The mucous membrane is covered with a mucopurulent exudate, and there are small petechial hemorrhages scattered about the tiny ulcerations. In any patient who has diarrhea with blood and mucus in the stool, careful examination should be made by the barium enema and by proctoscopy and sigmoidoscopy together with cultures and smears to determine the cause of the colitis. Late in the disease there is great dehydration because of the loss of fluid and acidosis because of the loss of the alkaline juices. Treatment should be directed against correcting the secondary effects of the disease. Since at times it is impossible to make an accurate diagnosis of the particular variety at fault, it is customary to put these patients on a medical regimen first. This will include dietary management, local antiseptic irrigations, succynilsulfathiazole, Sulfathalidine, penicillin in aluminum hydroxide gel, specific immunizing serums, for dysentery caused by the Shiga bacillus, and emetine because of the possibility of amebic dysentery. Last, in every instance a careful general physical examination should be made to rule out the possibility of tuberculosis or syphilis. In the presence of a stricture this is particularly important, and also the Frei antigen test should be done as well as biopsy to determine whether or not lymphopathia venereum is at fault.

Tumors of the Colon

New growths are common in the colon. They may be benign, such as lipoma, adenoma, and, more rarely, hemangioma and lymphangioma. By far the more important group of benign tumors of the large bowel produce a polypoid growth. Polypi may be due to fibroma, which are particularly common in the rectum, myoma, fibromyoma, and adenomyoma. Neurofibroma may be single or, in case of neurofibromatosis, they may be multiple. Other types of polypoid tumors are the adenomas, papillomas, or villous tumors, multiple polyposis, which has been described previously, and the inflammatory polyp. Also, more rarely, is the polyp which is said to be related to an allergic state and which is said to contain a great many eosinophils. Perhaps the most common benign neoplasm in the colon and rectum is the adenoma. This tumor usually begins as a sessile growth and the pedunculation comes as a result of the growth of the adenoma and a constant pull from the fecal current. The pedicle consists of normal mucosa and may become several inches in length, thus allowing the tumor considerable range of movement in the bowel. Histologically the adenoma may range from a tumor composed of almost normal mucosa to one of hyperplasia of the glandular elements as evidenced by branching tubules, multiple cell layers, and deep-staining nuclei. Sometimes the adenoma can be seen to contain cells which vary slightly in their staining reaction. The great danger of this growth is its liability to carcinoma. The virus tumor is much less common than the

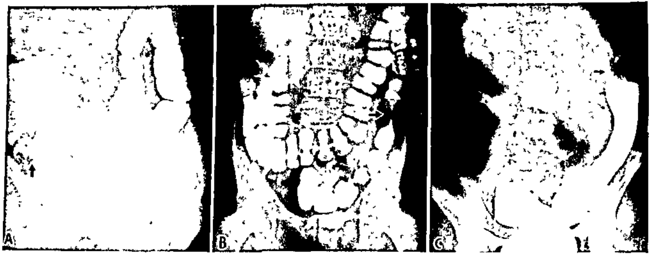

Fig. 313.—*A*. Carcinoma of the cecum (barium enema). Note the irregular filling defect in the cecal region. *B*. Carcinoma of the sigmoid (barium meal). Note the irregularity and narrowing in the upper sigmoid region, revealing the site of the carcinoma. *C*. Carcinoma of the descending colon just distal to the splenic flexure. Almost a complete obstruction is visualized by the barium enema.

adenoma. The papillomas attain great size and sometimes may be felt through the abdominal wall. They differ from carcinoma in that they are not indurated or ulcerated, and they do not invade the basement membrane. The liability of this type of papilloma to undergo malignant degeneration is so great that it is very often difficult to state even by microscopic examination whether or not the particular growth is or is not malignant.

The symptoms and signs of adenomatous polyp and a papilloma may be so similar that differentiation is impossible. Papilloma is almost never seen in children, whereas adenomatous ones are not uncommon. The symptoms and signs which are of greatest importance are: (1) bleeding which may be intermittent and which may be severe at times. The papilloma causes more bleeding than does the adenoma, although this is by no means always true. The blood may be bright red and free if it is low in the colon, or it may be mixed with the hard fecal mass if it is in the transverse colon, or it may be partially digested. Obviously the lower in the bowel the tumor and the more copious the bleeding the more bright red and the less mixed will be the blood in the stool. (2) Change in bowel habit. (3) Palpation of a tumor is sometimes possible.

The diagnosis is made by a careful digital examination in which the polypi in the lower bowel may be felt, proctoscopic and sigmoidoscopic examination for those in the upper rectum and lower sigmoid, and a barium enema or a contrast medium enema to demonstrate the polyps in the transverse colon, descending colon, and the cecum. The treatment is complete extirpation of the tumor together with a small portion of the mucous membrane. If there is any doubt concerning the malignancy, resection should be done. If the patient is properly prepared with sulfasuxidine and carefully cleansed with cleansing enemas the operation may be safely done. The large villous tumors in the rectum may require incision posteriorly in order to remove the growth. Frequently a large portion of the bowel must be removed with the growth because it is so large that it may completely encircle it. Multiple polyposis of the colon has already been described and its treatment discussed. In the adult multiple polyps may be removed if they are isolated and few in number. If they fill the bowel, of course colectomy is indicated.

Inflammatory polyps of the colon are due to prolonged ulceration from amebic dysentery or ulcerative colitis. Small islands of mucosa between the ulcers hypertrophy and become fibrotic, and they give the appearance of polypi. Some of them may be large, and they bleed profusely. Sometimes the polyp will develop a long pedicle, in which case it should be removed. Usually the disease has so destroyed the bowel that nothing short of colectomy will produce a cure.

The other types of benign growths in the bowel, as in the case of the polypi, are discovered either because of bleeding or because of intermittent obstruction. The polyp is notorious for this, since it may induce an intussusception or may occasionally become lodged in a narrow portion of

the colon. Also, this may be true of the large lipomas. In hemangioma, bleeding is a frequent complication. The diagnosis in each case is that of a solitary growth, and its nature cannot be determined preoperatively. The treatment in most cases is removal of the growth, and this is submitted to the pathologist for microscopic study. If benign, it is sufficient to excise the base and close the bowel in a transverse manner so as not to narrow its lumen. Hemangiomas, however, may require resection of the involved portion of the intestine.

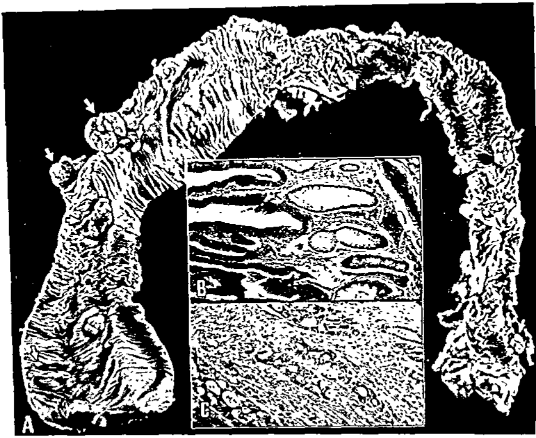

Fig. 314.—Acquired polyposis of the colon and carcinoma. *A*. Photograph of colon after total colectomy in a patient with acquired polyposis of the colon. Inset *C* is a photomicrograph of a resected carcinoma of the colon two and one-half years previously, and inset *B* is a photomicrograph of the present polypi within the colon which are benign. The arrows point to polypi throughout the entire colon. The healed scar of the previous resection may be seen in the extreme lower left. M. S. is a man 52 years of age who came to the hospital originally because of increasing constipation and an occasional streak of blood in the stool. Barium enema x-ray examination showed an obstructive lesion in the descending colon. At operation the descending colon was resected and an end-to-end anastomosis done. The neoplasm was an adenocarcinoma without involvement of the lymph nodes. The patient remained well for two and one-half years, after which he noticed occasional blood in the stools again. At this time a barium enema with air contrast technique revealed multiple polypi of the large bowel. Since these polypi were distributed from the cecum to the lowermost edge of the pelvic colon, a total colectomy was performed with the side-to-side anastomosis between the ileum and rectum. The lowermost portion on the left-hand side of the resected specimen was the site of the previous resection. There was no recurrence of the original carcinoma.

This illustrates the acquired type of multiple polyposis of the colon. The polyps were not present at the first operation and occurred within the two and one-half year period following the first procedure. It is easy to understand that, in this way, there may be carcinoma of the colon and then carcinoma at a later date or there may be multicentric carcinoma of the colon arising in the various polypi as shown in the gross specimen. (Case referred by Dr. H. Cahn.)

If a polyp is within the lower sigmoid or upper rectum so that it may be easily visualized with the proctoscope or the sigmoidoscope, it may be desiccated or removed with the snare. This should not be done where there is a broad base, because there is the danger of protracted bleeding. Desiccation is a very satisfactory method of destroying polyps that are within reach of the proctoscope or the sigmoidoscope. The danger of the benign polyp is that of carcinoma. It may begin as a patch of epithelial hyperplasia which occurs as a result of an inflammatory change or due to adenoma. Since the hyperplasia may become asessile and then pedunculated adenoma, there is a great chance of carcinoma being in one of these adenomas or the surrounding tissue. It is highly probable that a potentially malignant state which may or may not cause carcinoma may be present around an adenoma. It has been stated that a polyp may give rise to the "pile carpet" appearance and then traction due to the passage of fecal matter may cause a pedunculation to occur. The stem is filled with lymphoid tissue which is replaced by connective tissue, forming the stalk of the polyp. However, its transition into a malignant state can hardly be denied. Local excision of a solitary polyp which is malignant and which is not invading the rectal wall is sufficient provided that careful observation of the patient follows. However, radical operation should be performed if and when invasion of the rectal wall is discovered. For this reason it is perhaps judicious to remove the polyp with the knife rather than the cautery wherever possible.

Malignant Tumors of the Colon

Carcinoma of the colon is one of the most common types of cancer. About 50 per cent of all patients who die of cancer have the disease in the gastrointestinal tract and of these, five-eighths die of cancer of the stomach and approximately three-eighths die of malignant disease involving the colon or rectum. In other words, about 10 per cent of all deaths caused by cancer are traceable to malignant disease of the colon and rectum. Carcinoma of the stomach is the most frequent site of the disease and is followed in frequency by carcinoma of the colon and rectum. Cancer of the uterus and breast are third and fourth, respectively. Carcinoma of the colon and rectum is more common in males than in females. The incidence is highest in the sixth decade but a little earlier for women than men. The site of the growth in a combined survey of statistics from large clinics throughout the United States is as follows: the cecum, 6 to 8 per cent; the ascending colon, 4 per cent; the hepatic flexure, 2 to 3 per cent; the transverse colon, 4 to 5 per cent; the splenic flexure, 2 to 3 per cent; the descending colon, 3 to 4 per cent; the sigmoid, 13 to 14 per cent; the rectal sigmoid and rectum, 62 to 64 per cent. It would perhaps be better to speak in terms of the iliac and pelvic colon and pelvirectal juncture rather than the rectosigmoid. However, this is a rough estimate of the frequency of the site of the growth.

The cause of carcinoma is unknown. Much work has been done in an effort to evaluate a possible etiological factor. Some observers believe that a potentially malignant region exists in the colon prior to or coincidently with the development of cancer and that this region is larger than the growth itself. The region is the site of an inflammatory reaction, and the cells concerned are primarily mesoblastic, which are the natural defensive cells of the body, rather than epithelial. The effect on the epithelial cells is said to be secondary and represents a stage of destruction or impairment of nutrition followed by a stage of attempt at repair. If this repair becomes disordered and if the epithelium is isolated from the rest of the mucous membrane by a ring of lymphoid tissue as occurs

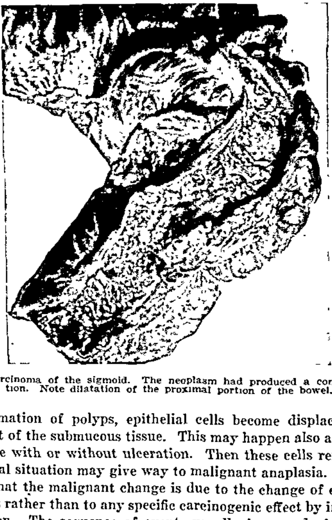

Fig. 315.—Carcinoma of the sigmoid. The neoplasm had produced a complete obstruction. Note dilatation of the proximal portion of the bowel.

in the formation of polyps, epithelial cells become displaced into the deeper part of the submucous tissue. This may happen also after rupture of a follicle with or without ulceration. Then these cells removed from their normal situation may give way to malignant anaplasia. One theory supposes that the malignant change is due to the change of environment of the cells rather than to any specific carcinogenic effect by inflammation or irritation. The sequence of events usually is a gradual histological transition from hyperplasia to adenoma or papilloma to carcinoma. Whether the inherent tendency to carcinoma is present in the cell is not known. Carcinomatous changes in papillomas can be diagnosed only by histological examination, and this must be based upon the observation of

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spread to the regional lymph nodes. Therefore, very often we are faced with the fact that an innocuous-appearing cancer may be removed completely, and the pathologist may report that there is no involvement of the adjacent lymph nodes, yet in such cases the growth may appear later in the liver from metastases which were present at the time of operation. Of course, there is no way of proving this unless the venous channels are carefully inspected by microscopic examination. Even here this may be impossible because the spread may be by embolism. In this way carcinoma of the colon resemble staphylococcic or streptococcic infection. The streptococcus creates very little local tissue reaction but invades the blood stream. The staphylococcus creates a great deal of local reaction and is therefore stopped by the local tissue response and the lymph channels. So it is with carcinoma of the colon. The innocuous-looking carcinoma very often is the invasive type which involves venous blood channels, whereas the large ulcerating type is one which is stopped by regional lymph nodes.

The Lymphatic Spread of Carcinoma.—The importance of this is well known and has been carefully worked up. The lymphatic spread of carcinoma of the colon is primarily embolic. The nodes where the emboli lodge will prevent further spread until they are overwhelmed. Further embolic spread is through collateral channels, each new node involved tending to make a longer and more difficult channel for the embolus to travel. The spread from node to node does not seem to be a common method of dissemination. Thus, the finding of a group of involved nodes within the field of surgery does not mean the case is hopeless, although it does mean that the chance for producing a cure following surgery is one-half as good as if the lymph nodes were not involved. The spread is primarily upward. However, in about 4 or 5 per cent retrograde metastases to nodes, anywhere from 1 to 5 cm., do occur. We have occasionally encountered metastases in the perineal wound and in the lymphatics extending downward into the perineum. The rectum has a lymphatic spread which may be divided roughly into the three areas supplied by the inferior, middle, and superior hemorrhoidal arteries. The inferior region is the 2½ cm. of anus proper, terminating superiorly at the pectinate line. The middle extends upward from the pectinate line to just above the insertions of the levatores ani muscles, and the superior extends from the point of the sigmoid colon and terminates approximately at the level of the third sacral vertebra. The lymphatics originate from a network of tiny lymph spaces which extend throughout the mucosa, submucosa, and the intramuscular layers. From the bowel wall the lymph spread is at right angles to the bowel, and from here into collecting trunks which proceed to the following areas: the inferior node regions may spread upward, joining the pathways of the superior area; occasionally it may go downward or caudally into the adipose tissue of the ischiorectal fossa. Therefore, the inferior and middle regions may spread upward or laterally or downward. The superior region is drained

tumor cells breaking through the muscularis. Many forms of polyps of the colon remain benign for years, but they cannot be trusted because most of them ultimately will become malignant. Thus it makes little difference whether the polyp was originally an adenoma or the result of an inflammatory change due to chronic ulcerative colitis or even diverticulitis. The fact remains that when the mucosa is thrown up into a polypoid formation, the danger of carcinoma is inherent.

Pathology.—Grossly three types of carcinoma are seen: polypoid, infiltrating or ulceratvie, and stenosing. These have been previously discussed under different captions as the well-differentiated adenocarcinoma, and these will vary to the undifferentiated carcinoma simplex. The medullary types of adenocarcinoma are present in 5 to 10 per cent. The scirrhous type causes a stenosis and has given rise to the name of the "napkin ring" deformity of the large bowel. The pathological type of carcinoma is important not only because of its tendencies to growth, but also because of the symptoms and signs. For example, the encephaloid or medullary type of carcinoma, which is a fungating mass, is infected very early and produces ulceration, thereby causing an inflammatory reaction of the lymph nodes. This may be mistaken for involved nodes with carcinoma which may not be the case. This type of growth also is apt to produce bleeding, and gross hemorrhage may occur. Contrariwise the scirrhous type of carcinoma is apt to produce very few symptoms except a change in habit time. Later the symptoms may be chiefly obstructive and no bleeding will occur at any time. Carcinoma may spread primarily in one of three ways or in a combination of these ways: (1) by local extension from its site of origin, (2) by invasion of venous channels, and (3) through the lymphatic system. Most of the growths are low grade, and there will be considerable local growth before widespread metastases has occurred. However, local extension is frequently a cause for inoperability. It may include contiguous organs such as the bladder, the uterus, the tubes, the ovaries, the broad ligaments, the peritoneum, and the contiguous loops of bowel. In many cases in which we have thought that involvement of contiguous organs was present we have found that it was really an inflammatory process rather than a neoplastic one. This is particularly true of the bladder and the uterus due to the ulceration which occurs at the rectosigmoid. Inflammatory changes are common. Perforation may have occurred and the growth may have become densely adherent to the uterus in front or of the bladder in the male. Very often combined resection of the colon, including a portion of the bladder or the uterus, will reveal at examination that the adhesion has been duo to inflammatory change and that the new growth has not actually extended into the adjacent organ.

Venous Spread of the Disease.—Venous spread makes operation impossible for complete extirpation of the growth. It has been noted that when vascular invasion takes place that this occurs before the disease has

conservative operations upon the rectum and the sigmoid with preservation of the sphincter. Since lateral dissemination does occur, the segmental resection of low carcinoma is extremely hazardous in that it may not remove all of the carcinomatous tissue. By lateral dissemination we mean that which spreads along the levatores ani muscles, the coccygii, the base of the bladder, the cervix, or the base of the broad ligaments, to terminate in the internal iliac nodes. This discussion is practical because it deals with the applicability of so-called sphincteric preservation operations. Lesions which are partially or completely below the peritoneal reflexion have a high incidence of local and liver recurrence and, therefore, pull-through or sleeve resections may not produce a cure. Such operations are justified only if the bowel and lymphatic tissue are resected at least 4 to 5 cm. above and below the growth.

The grading of carcinoma of the bowel is based upon several factors:

1. Broder's classification which has been described in Chapter 15 deals with the type of cell and the number of cells which are of an abnormal nature. In grade 1 carcinomas the cells are columnar and the nuclei are not prominent and are smaller than in grade 2. In grade 2 the cells are less columnar and the nucleus assumes a more prominent part in the cell. The nuclei are larger. In grade 3 the cells are larger and round, and the nucleus takes nearly all of the cell. In general, the cells in grade 4 lesions tend to be large, hyperchromatic, and round and have little resemblance to normal cells.

2. Duke's classification is based upon three factors which were originally described by Lockhart-Mummery which he grades as follows: Class A, by which he meant small movable lesions which do not appear to involve the muscular coat or the lymph nodes; Class B, lesions which appear to involve the muscular coat but are not fixed and the lymphatic involvement is not extensive; and Class C, large growths which are fixed and which have extensive lymphatic involvement. Duke's classification is modified so that in Class A are the lesions which were definitely limited to the wall of the rectum without extrarectal extension or metastases to lymph nodes; class B, growths which have spread by direct extension to extrarectal tissues but have not apparently invaded the lymph nodes; and Class C, all carcinomas in which metastases are present to the regional lymph nodes. By grading carcinomas in Broder and Duke's classification a more accurate idea as to prognosis may be obtained. For example, it is apparent that a grade 4 carcinoma has a very poor prognosis and will usually also be a grade C Duke's classification. However, if it is a grade 4 Broder's and a grade A Duke's, the prognosis is better than if it is a Broder's grade 4, grade C Duke's. And the reverse is true. Namely, a Broder's grade 1 which has already extended beyond the confines of the rectum has a poorer prognosis than a grade 4 which is still localized. The presence or absence of mucus is not in itself a guide to prognosis, although mucin, which is produced by the cells, in general,

into nodes which roughly follow the branches of the superior hemorrhoidal artery. After perforating the rectum, they run obliquely upward and backward to reach the nodes in the mesorectum. They traverse several small nodes placed on the muscular layer and covered by the fibrous coat of the rectum on their way. These are known as the pararectal nodes of Gerota. These nodes are found especially in the region of the ampulla. The lowest one is immediately above the levator ani. Normally the lymphatic drainage of the superior region is only upward, although, as has been said, occasionally in blocked lymphatics a retrograde spread

Fig. 316.—Carcinoma of the rectum (polypoid type).

may occur. Carcinoma from the anus or rectum may spread up to the sigmoid by intramural extension and invasion of the small lymph nodes within the bowel wall. Marginal extension may also occur, around the bowel as well as *within the bowel. However,* extension is limited, and, as a rule, intramural dispersion is not of great importance. But in the eradication of the carcinoma, a liberal margin should be *taken* with the growth proximally and distally, say at least 3 to 4 cm.

By far the most important manner of spread is that of extramural dissemination. *Recently the study of extramural spread* has been subjected to close scrutiny because of the revival of conservative or so-called

conservative operations upon the rectum and the sigmoid with tion of the sphincter. Since lateral dissemination does occur mental resection of low carcinoma is extremely hazardous in th not remove all of the carcinomatous tissue. By lateral dissemi mean that which spreads along the levatores ani muscles, the the base of the bladder, the cervix, or the base of the broad lig terminate in the internal iliac nodes. This discussion is practic it deals with the applicability of so-called sphincteric preservati tions. Lesions which are partially or completely below the reflexion have a high incidence of local and liver recurrence a fore, pull-through or sleeve resections may not produce a cu operations are justified only if the bowel and lymphatic tiss sected at least 4 to 5 cm. above and below the growth.

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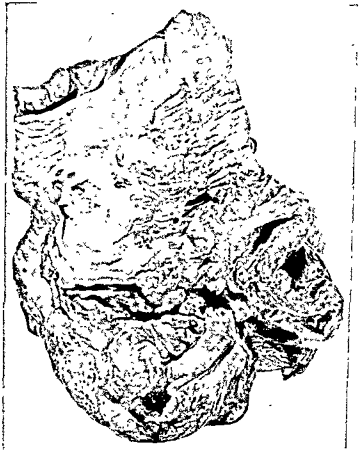

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gives them a primitive function which would tend to imply that the growth was of a lesser degree of malignancy than one which had no *function at all.* Since, however, many carcinomas have a mucoid degeneration and since the cells may be highly malignant and may have spread the presence of mucus, this loses its importance in prognosis.

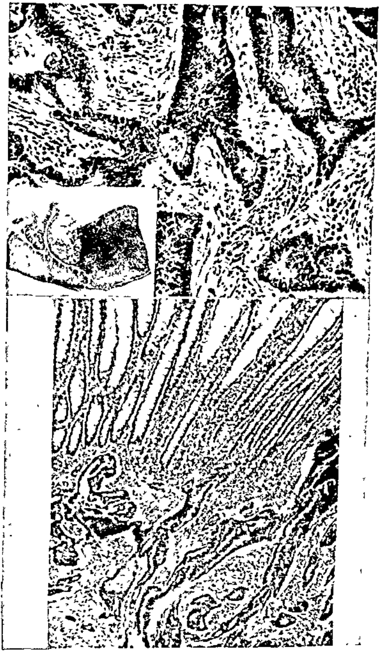

Fig. 317.—Carcinoma of the rectum. *A.* The low power shows the abrupt transition of the normal gland structure into malignant distortion. The high power shows the downgrowth of cylindrical cells. Some contain colloid. *B.* Medium power, showing the tubular downgrowths of atypical epithelium into the submucosa.

Tumors of the higher grade are more rapid in growth and their metastases are apt to cause the death of the person earlier than those of the lower grade. It is perhaps well to grade carcinoma of the rectum in

both classifications when attempting to evaluate it from the prognostic point of view. Carcinomas of the large intestine may be multiple. Many cases have been reported in which the carcinoma has been removed only to have growths appear in other parts of the large intestine. Obviously the immediate deduction in such cases is that the original carcinoma was not completely removed. However, a sufficient number of cases have been reported in which a growth arose in a different location from the primary growth and which was responsible for its own metastases and which had different pathological pattern. Often pólypi which have been overlooked are responsible. Also, it is remarkable the number of cases in which multiple carcinoma may arise from different organs. We have recently encountered a woman who had a carcinoma of the iliac colon. This was resected and an end-to-end anastomosis was done. It was grade 3 Broder's, grade B Duke's classification. The prognosis was not good. In six months the patient returned to the hospital with a large tumor in the abdomen. At operation a proliferating papillary cystadenocarcinoma of the left ovary was responsible for the condition of the patient. This had metastasized over the entire visceral and parietal peritoneum. Multicentric carcinoma then may occur within the organ itself as in the colon or may occur in various other organs. There seems to be no explanation for this observed fact.

Symptoms and Signs of Carcinoma of the Colon.—The complications of carcinoma such as ulceration, hemorrhage, and stenosis of the intestine bring the growth to light rather than the symptoms of the growth itself. In either right or left colon, carcinoma usually gives rise to some abdominal distress and a change in bowel habits, and sometimes a mass may be felt in the abdomen. There may be a weight loss, although this may not be present until extremely late. Blood in the stools is present in approximately one-third of the patients, but since the most common cause for blood in the stools is internal hemorrhoids, this is often not considered seriously. The two sides of the bowel give different sets of symptoms. On the *right* side, the chief finding may be a slight change in bowel habit, some abdominal distress, extreme weakness, and a severe anemia with mild systolic murmur, probably anemic in origin. Very much later a tumor may be discovered. On the *left* side the carcinoma is apt to cause an early type of obstructive symptoms, and therefore the change in the habit time is most important. There may be blood in the stools. The diagnosis is frequently made by the palpation of a tumor or by discovering the growth by digital rectal examination. The fact that in practically one-third of the carcinomas of the lower bowel the neoplasm may be palpated by the examining finger makes it mandatory for every patient to have a routine digital examination of the rectum. There may be some tenderness which will lead to the suspicion, although this is also true of diverticulitis, and this cannot be relied upon. The same thing is true of occult blood, although it lends support to the diagnosis. Barium enemas are

excellent except that the segments where the growths usually occur are in the lower sigmoid, and here the x-ray will miss 10 to 15 per cent of the carcinomas. Proctoscopic examination with biopsy is the method of choice. Any change in the bowel habits of a patient (whether increasing constipation or alternating constipation and diarrhea) or the occurrence of persistent, marked gurgling sounds makes the physician suspicious of new growth.

Vomiting does not occur until very late due to the fact that the ileocecal valve withstands great pressure. The blood supply of the large bowel is different from that of the small bowel in that the vessels almost encircle it before entering its walls. In the small bowel the vessels dip in between the muscularis and submucous coats nearer the mesenteric border; consequently the large bowel may become greatly distended without gangrene or perforation. This is not true of the small intestine.

Carcinoma of the cecum produces toxic symptoms and profound anemia rather than mechanical symptoms. This anemia has been attributed to (1) bleeding; (2) injury of the mucous membrane, with loss of its selective absorption powers, leading to toxemia; (3) increase in the normal retrograde waves, favoring increased absorption; (4) the large size of the growths on the right side, due to the larger space for growth, and the ulcerating character of these growths.

If, in addition, there is blood in the stool, the physician thinks of carcinoma of the rectosigmoid or rectum. The diagnosis is made by digital examination (for the low type), proctoscopic examination, and barium enema with x-ray plate. The last is the most important.

Prognosis of Carcinoma of the Colon.—Theoretically the prognosis of carcinoma of the colon should be good. This is true because (1) the development is slow, (2) invasion of the lymphatics is delayed, (3) generalized metastasis is rare, and (4) mucoid degeneration rather than rapid cell proliferation is the usual course. However, this latter point is determined by the type of cell rather than the presence or absence of mucus. The lymph nodes lie close to the colon, as has been shown, forming a first line of defense. Injections of the lymph vessels by Gerota show that they follow the larger blood vessels. Therefore, an operation to be adequate must include not only the lymph vessels but contiguous tissue and approximately three inches on each side of the growth as well in order that a complete extirpation be achieved. If this is done and if the lymph nodes are not involved, a five- to ten-year survival rate of over 70 per cent is feasible. However, where the lymph nodes have been involved, this survival rate drops to approximately 35 per cent. On the right side, however, even with the lymph node involvement the prognosis is much better. In general, it may be stated that nowhere in the body may carcinoma offer such a good prognosis as in the colon, particularly on the right side. However, here, as elsewhere, the growth must be diagnosed early enough so that all contiguous tissue and lymph node basins may be removed.

Treatment of Carcinoma of the Colon.—The treatment of carcinoma of the colon depends upon its location and complicating factors plus the general condition of the patient. First, the uncomplicated carcinoma in patients whose condition is good demands careful preoperative preparation and resection of an adequate amount of the large bowel. The preparation includes the following: attention to water balance, blood volume restoration, the use of Sulfasuxidine or Sulfathalidine for a period of eight days to reduce the flora of coliform bacteria, the use of vitamin K which is not synthesized with the use of Sulfasuxidine, proper food which is low in residue, high carbohydrate, high protein diet, attention to vitamin requirements, and, last, careful cleansing of the bowel prior to operation.

If the carcinoma is in the *cecum*, then the cecum, ascending colon, and the hepatic flexure should be removed and ileotransversostomy done. In the *transverse colon* this portion of the bowel is removed from the hepatic to the splenic flexure. The *splenic flexure* requires removal of the transverse colon for a distance of approximately three inches proximal and the same distance distal to the growth. The *descending colon* requires removal of the sigmoid as well and anastomosis between the splenic flexure and the pelvic colon just above the reflexion of the peritoneum. The *rectosigmoid* may, under certain conditions, be segmentally resected with an end-to-end anastomosis. If, however, there are any complicating factors or extensions, *abdominoperineal* resection may be necessary. This will be discussed later. The growths which lie above 10 cm. from the pectinate line are usually resectable by segmental resection with end-to-end anastomosis. The normal rectum in the adult is anywhere from 13 to 15 cm. in length. However, the peritoneal reflexion varies, and this is an important consideration in primary healing because resections done below the 10 cm. level require extensive mobilization, and there may be a sloughing of the suture line—this, in addition to the fact that the rectum does not have a serosa. The consideration, however, is not whether a sphincter may be preserved or whether segmental resection may be done; the important fact to decide is whether or not it may be adequately performed so that all of the carcinoma and the involved lymph nodes may be removed. Certainly in grade C and even in grade B growths, segmental resection below the 10 cm. level are dangerous and probably will not give the greatest number of five- to ten-year survivals. Recently there has been a revival of the old Hochenegg or pull-through operation, also known in German as the Durchzug operation. This operation is done by mobilizing the bowel proximal and distal to the growth, removing it, and bringing the upper segment down through the lower segment in an effort to preserve sphincteric action. This is often successful. Also, another method recently described is a combination of the Whitehead and the pull-through operation. With this method the sphincter is dissected away, the entire lower bowel is removed, including the carcinoma, and the upper segment is brought out through

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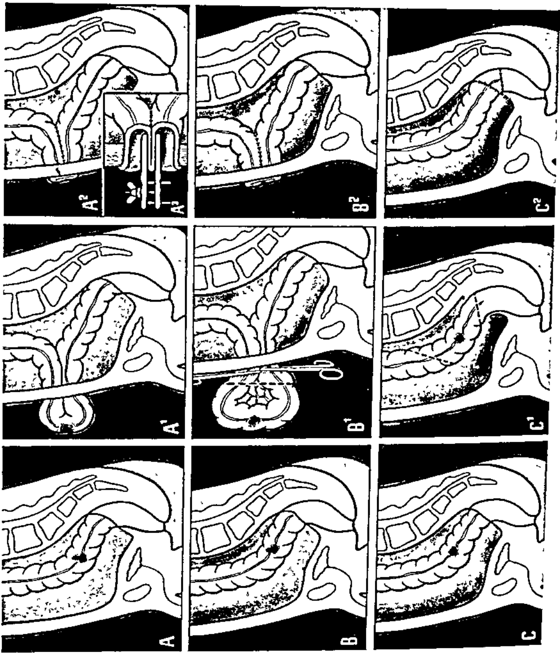
Fig. 318.—Intraabdominal types of operations for carcinoma of the rectum and rectosigmoid. *A*. The Mikulicz operation. The involved sigmoid is exteriorized, A^1, and later it is removed, A^2; then crushing clamps are applied through the spur which had been made, converting the double-barrel colostomy into a single opening, A^3. Later, the opening is closed, re-establishing the continuity of the bowel. *B*. An obstructive type of intraabdominal operation developed by Rankin. Here the bowel is exteriorized, clamps are applied, and the carcinoma is removed at once. B^1. The two loops have been anchored together, forming a spur. The clamps are removed after forty-eight to seventy-two hours. The spur is then crushed, thereby restoring the continuity of the colon. Later the protruding end of the bowel is closed. *C*. Sleeve resection. If the carcinoma is high in the pelvic colon, it may be completely removed with sufficient bowel below for side-to-end or end-to-end anastomosis. The latter may be safely accomplished by dividing the colon obliquely, to provide an adequate lumen, C^1. The peritoneum is then brought down above the suture line, C^2.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resections of the rectosigmoid, anastomosis is made to the rectum which does not have a serous coat. Therefore the peritoneum is attached above the suture line, and a Penrose soft rubber tube is placed anterior to the coccyx to drain the perirectal space. Occasionally this will be followed by a fistula for a short period of time. If the patient is maintained on Sulfasuxidine, this will soon close spontaneously. We have not as yet had to excise such a fistula. Drainage is required also because the perirectal tissues lying below the pelvic perirenal floor are highly susceptible to infection, and also sometimes much trauma is induced in gaining access to this region. Therefore, drainage is routine procedure and may require resection of the coccyx to obtain better drainage. In this region end-to-end anastomosis is usually practiced and may be done safely. We have not encountered a stricture at this area. However, if the bowel is small, it may be better to close the proximal end and do a side-to-end anastomosis between the side of the upper segment and the end of the lower. This will prevent any tendency toward stricture formation. These operations may be done by the open technique because of the careful preparation which may be attained by Sulfasuxidine and Sulfathalidine. Complimentary cecostomy is not necessary but is useful in very low resection and primary anastomosis. This is particularly true in the old, in whom it is undesirable to limit food and fluid by mouth for long periods of time. (See Fig. 318.)

Posterior resections may be done by removing the coccyx and a portion of the sacrum. In this operation the coccyx and the fifth and half of the fourth sacral bodies are removed. The pelvic fascia is divided and the dissection is carried around the circumference of the rectum outside the perirectal fascia. The peritoneum is opened on the anterior surface, and sufficient sigmoid is drawn down with which to do a repair. Then the peritoneum is reattached by sutures and the bowel further mobilized, and an end-to-end anastomosis is done. The area is then drained with a soft rubber tube, and no colostomy is required in these cases. The operation has some strong advocates but is usually frowned upon because again there is the danger of not getting all of the growth and not being able to do a thorough abdominal exploration. (See Fig. 319.)

The most widely employed operation for the lower portion of the pelvic colon and the rectal ampulla is the so-called Miles operation, or the one-stage abdominoperineal resection. This procedure is carried out through a left oblique incision. The bowel is inspected carefully and then mobilized by incising the lateral margins of the mesosigmoid. Wide areas may be resected, including the superior hemorrhoidal lymph channels and nodes as well as the middle and inferior hemorrhoidals. The entire sacral region and the lateral perirectal tissues may be removed after the ureters have been identified and pushed aside. The proximal end of the bowel is then brought out through the upper margin of the oblique incision or through a separate wound. The pelvic peritoneum is sutured. Then the abdomen is closed. The patient is then put up in the lithotomy position and the entire anus, including the sphincters and all perirectal tissues, are

the preserved sphincter. The special features of this procedure include a dissection of the sphincter as is done in the Whitehead operation for hemorrhoids; then the sphincter muscle is divided posteriorly, and the mobilized bowel which has been freed from above, preserving the blood supply, is brought down through the divided sphincter. Later the sphincter may be closed. The desirability of preserving the sphincter is admitted by all, but not at the expense of complete eradication of the growth. Therefore, we may say that in the lower sigmoid above 10 cm., segmental resection anteriorly done is a feasible and very logical operation in the class A types of carcinoma. It may also be feasible in carcinomas at lower levels. However, to employ this method in all types is feasible surgically but is not to be regarded as giving the best results insofar as five- to ten-year survivals are concerned. (See Fig. 320.)

The *complicating factors* of *carcinoma* include obstruction, fixation, and infection. Carcinoma with obstruction, fixation, or infection (that is, infection within the growth) makes immediate resection undesirable. If carcinoma is producing obstruction, often after the administration of large doses of sulfasuxidine the infection may subside to such a degree that the normal channel will become patent enough to permit the normal fecal current to drain. In acute obstruction, however, it may be necessary to do a temporary cecostomy or appendicocecostomy, or if the obstruction is at the cecum, an ileostomy may be necessary. If the obstruction is not complete and usually it will not be on the right side, a preliminary ileotransversostomy should be done, and then at a second stage the growth may be removed together with the terminal ileum, ascending colon, and a portion of the transverse colon. This will not often be necessary, particularly if a preliminary ileostomy has been done. In such cases after adequate drainage and preparation with sulfasuxidine, second stage operation usually includes resection and anastomosis.

Carcinoma of the *transverse colon* with obstruction may be treated by *a preliminary cecostomy. In doing a cecostomy, a word of warning should* be sounded. The tube introduced should be large, being approximately one-half inch in diameter. We have frequently failed to obtain the proper drainage by using small tubes through an appendicocecostomy. The colon may then be washed out by using a balloon type or Miller-Abbott tube type for irrigation which makes it possible not only to irrigate the proximal portion of the bowel but also to introduce Sulfasuxidine, thereby partially degerminizing it. Then at a second stage the transverse colon may be resected as previously indicated. In obstruction of the splenic flexure it is perhaps best to do a transverse colostomy. Then at a second stage resection is done. It is probably true that the closer to the obstructed portion that the colostomy is made, the more complete will be the emptying of the proximal loop. Therefore, a transverse colostomy is useful in the presence of an obstructing lesion of the splenic flexure. The same may be said for an obstruction in the descending or sigmoid. The reason that the colostomy is not made lower is that it interferes with the secondary operation. In

Fig. 319.—Diagram illustrating various types of operations for carcinoma of the rectum and rectosigmoid. This diagram and the two which follow show the various types of operations. This figure depicts the perineal and sacral operations. *A*. Perineal excision with anastomosis. *A^1*. Lines of excision. The coccyx and a portion of the sacrum have been removed. *A^2*. End-to-end anastomosis. *B*. Preliminary colostomy. *B^1*. Perineal excision with closure of the distal segment. *B^2* The distal segment is brought out through the perineum to prevent a blind pouch accumulation. *C*. Kraske type of perineal excision. *C^1*. A portion of the sacrum as well as the coccyx is removed, and through a perineal approach the carcinoma is excised and the remaining bowel anastomosed as shown in *A^1*. *C^2*. In the Kraske operation the proximal end of the rectosigmoid may be brought out as a perineal anus—an undesirable procedure.

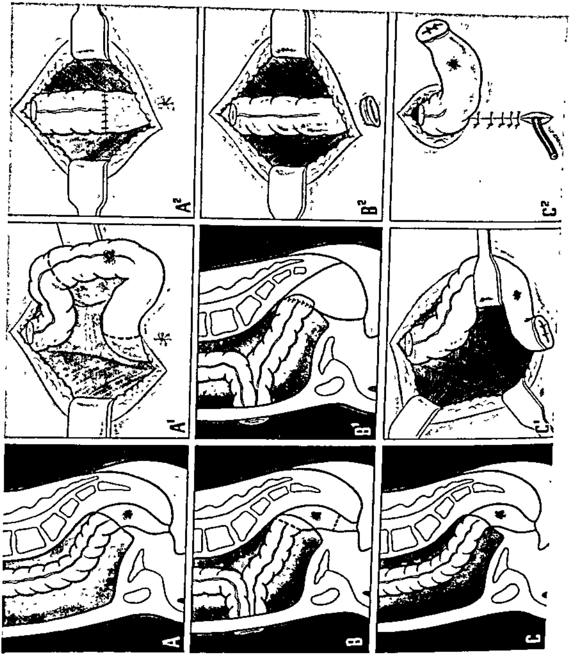
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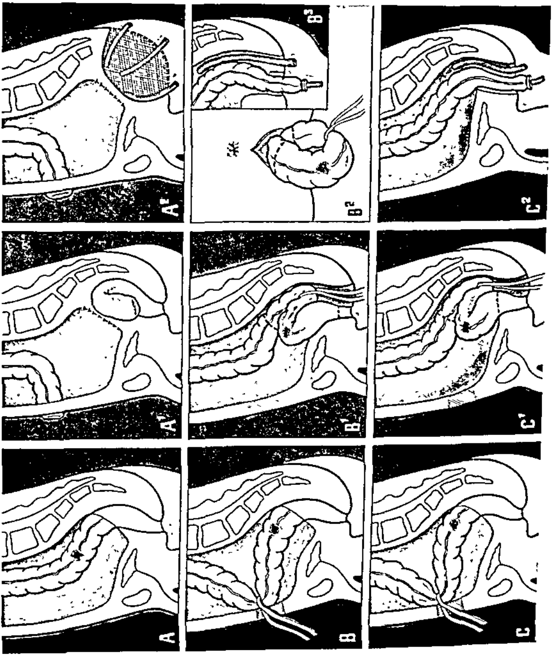
Fig 320.—Combined abdominal-perineal operations for carcinoma of the rectum or rectosigmoid *A*. The Miles operation. *A*[1]. The abdominal portion of the operation has been completed. The divided sigmoid has been placed beneath the reconstructed pelvic floor and a colostomy has been formed *A*[2]. The perineal part of the operation. The sigmoid, rectum, and anus have been removed and drains have been placed in the perineal cavity. The operation may be performed in one or two stages.

B. The Babcock operation. The iliac and pelvic colon have been freed through the abdominal incision. *B*[1]. The perineal part of the operation. The freed colon and rectum are brought out through a perineal incision. *B*[2]. The colon and rectum are removed down to the sphincter which is split posteriorly *B*[3] The proximal colon is brought down through the sphincter.

C. The Hochenegg or "durchzug" operation The abdominal part is shown. *C*[1]. The sigmoid is brought out through a perineal incision and removed, leaving a cuff of rectum *C*[2] The proximal colon is brought down through this small portion of remaining rectum and out through the sphincter.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surgery. The suture lines are carefully placed without tension and with preservation of blood supply and careful approximation of serosa to serosa wherever this is possible, and, if impossible, then the peritoneum is attached above the suture line. In order to avoid obstruction, openings in and around mesenteries are carefully closed, particularly the area between the extruded proximal colon and the lateral pelvic wall. Also, all raw surfaces must be covered. Loops of small bowel will become adherent to the reconstructed pelvic floor if the serosa is not sutured to serosa, producing a smooth suture line. Other complications which are not specific for this type of operation include embolism which does occur in a limited number of patients. Bladder complications are more common, but since the introduction of early mobilization so that patients may empty the bladder without the aid of catheters, this has been greatly lessened. (See Fig. 320.)

The Mikulicz type of resection has a limited place in surgery of the colon for cancer. It is useful in badly infected colons in which the diagnosis is more or less by surprise. The carcinomatous area of the bowel is mobilized and brought outside the abdomen through a separate incision or through the incision which has been made to do the exploration. This may be left on the oustide and removed at a later date, or the proximal and distal ends of the bowel may be sutured together, forming a spur, and then an obstructive resection may be done; that is, clamps are placed on the proximal and distal parts of the bowel and the carcinoma removed. At a later date a clamp is placed between the two loops which have now formed a double barrel shotgun type of colostomy, and then at a third stage the bowel is closed. This type of procedure has not given good results but was an important step in the treatment of infected carcinomas before the era of chemotherapy and antibiotics. It still is useful in so-called surprise cases, where the element of obstruction is present and where the carcinoma has already caused a perforation and the whole part must be extruded. The dangers of the operation are the local infection and, most important, the transplantation of the carcinoma into the skin at the site of the colostomy. Therefore, at present, if operation is contemplated, this type of procedure is not employed as commonly as was formerly the case. It was even employed in dealing with carcinomas of the right side at one time. In all cases of carcinoma the postoperative management consists of the use of a Levine tube to delimit the amount of gas in the upper intestine unless a preliminary colostomy or complimentary colostomy has been done. The use of Sulfasuxidine is not usually continued after surgery. Penicillin is given in fairly large doses, 100,000 units every three hours. Streptomycin is employed in a dose of .2 to .5 Gm. every six hours, giving a total of .8 to 2 Gm. per day. This is thought to reduce the incidence of coliform infection. Attention is also given to water balance and plasma and blood volume, and then a careful dietary management is maintained until healing has occurred. This consists of a high protein, high carbohydrate, low residue diet. In the Miles operation or the abdominoperineal resection the colostomy sometimes requires correction in that the loop of bowel may

completely excised and the loop is brought out from below. The lower margin is left open with a few soft Penrose drains. Packs are not employed because the gauze is apt to adhere to the suture line of the peritoneum, and in removing them this may be torn, producing hernia or peritonitis. Within ten days to two weeks these patients are up and around, and they are permitted to sit up on the second day. The perineal wound heals slowly but completely. In the hands of most surgeons this operation has given the most satisfactory result. Its objection is, of course, the use of the abdominal anus or the permanent colostomy. However, with proper education and careful dietary management the stool may be regulated so that it will be loose or hard, depending upon the type of food that is eaten. Furthermore, colostomy bags are available which are not too unsightly and which may be cleansed without much trouble. Most patients learn to regulate their dietary habits so that the stool is kept formed and so that by using a syringe to irrigate the colostomy once or twice a day they do not require a colostomy bag during the day. Instead they wear a pad and have very little trouble.

The operation of abdominoperineal resection may be combined with resection of the uterus including the posterior vaginal wall. Also, a portion of the bladder may be resected, and, if necessary, the entire bladder, performing a preliminary ureterostomy. This is a very extensive procedure and may not result in a cure but may be done in the extreme case where it seems indicated. Also, in a few instances a single nodule in the liver may be resected, doing even a lobectomy of the liver if that is necessary. These radical resections may not result in many cures. However, they will prolong life and ameliorate suffering, and in that sense they are to be advocated in selected cases. Usually, however, where there is extensive invasion of the bladder, particularly low down in the prostate, cure is almost impossible and, therefore, a palliative colostomy is done. In all massive resection of this nature in which a portion of the bladder is removed a suprapubic cystotomy is done. Also, a complimentary transverse colostomy is performed to relieve the tension on the suture line. End-to-end anastomosis may be accomplished in connection with this operation, but as a rule it will be an abdominoperineal type of resection. One may question these heroic methods of excision. However, if the surgeon is worthy of his tradition he will do as radical a procedure as is commensurate with the patient's ability to stand the surgery with the hope of producing a cure or an arrestment of the disease. If he can save only 1 or 2 per cent of such hopeless cases, he is better off than if he did not try at all. If the operation is carried out properly, there will be only a few complications. However, there are inherent dangers in the operation and the most formidable of these is peritonitis, or obstruction. Peritonitis has been greatly reduced due to the advent of the sulfonamides and careful aseptic technique; that is, as near aseptic as possible. Surgeons have learned that they cannot depend upon drugs as a substitute for careful atraumatic

surgery. The suture lines are carefully placed without tension and with preservation of blood supply and careful approximation of serosa to serosa wherever this is possible, and, if impossible, then the peritoneum is attached above the suture line. In order to avoid obstruction, openings in and around mesenteries are carefully closed, particularly the area between the extruded proximal colon and the lateral pelvic wall. Also, all raw surfaces must be covered. Loops of small bowel will become adherent to the reconstructed pelvic floor if the serosa is not sutured to serosa, producing a smooth suture line. Other complications which are not specific for this type of operation include embolism which does occur in a limited number of patients. Bladder complications are more common, but since the introduction of early mobilization so that patients may empty the bladder without the aid of catheters, this has been greatly lessened. (See Fig. 320.)

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be too long. It is desirable to have this the case rather than too little exteriorized bowel with ultimate retraction of the permanent colostomy. This latter may require further operation. *Carcinomas below the peritoneal* reflection recur more frequently than those above. This recurrence manifests itself with a persistent progressive pain described as "bursting pain" by the patient.

THE RECTUM AND ANUS

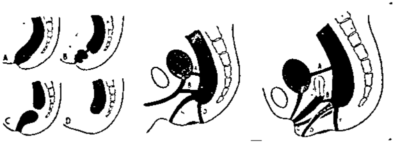
The rectum extends from the dentate margin to the peritoneal reflexion. The anus extends from the skin to the dentate margin. The anus varies in length from 1½ to 3 cm. Its superior border is the dentate margin which comprises the anal semilunar valves and the anal papillae together with the *anal clefts or Morgagni*. The dentate margin is also known as the pectinate line or the anal rectal line and the muco *cutaneous line or border. The term white line of Hilton* has been used to refer to the intersphincteric line and is not synonymous with dentate margin. The anal canal is lined by skin and not by mucous membrane. The anal papilli form the ridges in the anal clefts or valleys which appear at the dentate margin. The rectum is, of course, lined by mucous membrane and, therefore, the dentate margin has been called the mucocutaneous line or border.

The hind gut in the early embryo ends in a blind pouch which is later joined by an invagination of the proctodeum (anus). As a result of this embryological arrangement, many congenital anomalies occur. Then, too, the urogenital tract in the embryo is part of the common cloaca which is separated later into an anterior urogenital sinus and a posterior rectum by a saddlelike partition (urogenital septum). Should this fail to close completely, various fistulae may occur. These fistulae may be between the rectum and the vagina, or the rectum and the bladder, or the rectum and the urethra. The anomalies include an imperforate anus in which a thin membrane covers the anal *opening, congenital absence of the anus or rectum, persistence of a blind hind-gut*, and various strictures and fistulae.

Anomalies are discovered first by a careful inspection of the child at birth. In the congenital absence of the anus, this is apparent and *if, in* addition, it is seen that there is meconium coming from the urethra, a *fistula is, of course, suspected. In all cases where there is distention* in the absence of flatus or meconium a scout film of the abdomen *should be made*. This may be facilitated by taking a picture of the baby in the upside down position to determine the lowest level of gas.

The operation for the relief of the condition is planned *according to* the position of the blind pouch. If the hind-gut is within approximately a centimeter of the skin margin, it may be brought down by an operation done entirely from below. In such cases, particularly *when there is a* sphincter present, an incision is made through the sphincter in the midline, dividing the upper half of the sphincter. The blind hind-gut is mobilized and brought down and sutured to *the skin. If, however*, there is only a persistent anal membrane, no mobilization is necessary and division of this membrane is all that need be done. When the hind-gut is high, it may be better *to wait twenty-four hours or* more to allow gas to come down to its lowest level. In this way the x-ray examination will be more accurate and will reveal the true level of the blind hind-gut. *If the hind-gut is*

high, that is, more than a centimeter or a centimeter and a half from the anus, then it is, perhaps, best to do a colostomy. The colostomy should be done in the transverse colon and it should be an exclusion type; that is, the two loops should be separated by a bridge of skin. If this is not done, the distal loop or the blind loop will fill with fecal matter spilling over and fistulae will remain, or if they have been potential, they will open up. There is one warning about the transverse colon in the newborn. It may upset water balance to such a degree that a long period of time cannot be allowed to elapse before the second operation is done and, therefore, when a transverse colostomy is done, preparation should be made to do the combined abdominal perineal mobilization technique within a relatively short time; namely, within a week or two or sooner if there is difficulty in maintaining water balance. If the child is in a very precarious condition and if the blind loop is extremely large, it is perhaps best to bring the loop up to the skin and make an opening, using a catheter, and suturing the catheter by purse-string suture. It is very hazardous to attempt to bring the descending colon which is greatly dilated out through the abdominal opening to make a loop colostomy because the hind-gut is too thin and it will



I. *II* *III.*

Fig. 321.—Diagram illustrating types of congenital anomalies of the rectum and anus. *I.* Four common types of anomalies. *A*, occlusion by anal membrane or skin; *B*, narrowing at the anal margin or higher; *C*, anus and anal pouch normal but hindgut ends blindly; *D*, absence of anus with blind hindgut. *II.* Fistulas in the male with or without anomaly of the rectum or anus: *A*, rectovesical; *B*, rectourethral; *C* and *D*, rectoperineal. *III.* Fistulas in the female: *A*, rectovesical; *B*, rectovaginal; *C*, recto-fossanavicularis; *D* and *E*, rectoperineal. (After Berman. Surg., Gynec. & Obst. 66: 11, 1938.)

tear and it is too large to be mobilized. The combined abdominal and perineal technique should not be attempted without a preliminary colostomy in most cases. Rarely there will be so little distention that it will be safe to attempt this without preliminary colostomy. Fistulae may be closed at the time that the combined operation is done. At a later date the colostomy may be closed.

Prolapse of the rectum may affect the mucous membrane alone or the entire wall. The term *procidentia* has been applied to the latter condition. In the young infant a prolapse of the mucous membrane is not uncommon, particularly in association with congenital anomalies of the spinal cord or with extrophy of the bladder. The condition may be troublesome but usually responds to replacement and strapping of the buttocks together with adhesive tape between defecations. Within a few weeks the mucous

be too long. It is desirable to have this the case rather than too little exteriorized bowel with ultimate retraction of the permanent colostomy. This latter may require further operation. Carcinomas below the peritoneal reflection recur more frequently than those above. This recurrence manifests itself with a persistent progressive pain described as "bursting pain" by the patient.

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The operation for the relief of the condition is planned according to the position of the blind pouch. If the hind-gut is within approximately a centimeter of the skin margin, it may be brought down by an operation done entirely from below. In such cases, particularly when there is a sphincter present, an incision is made through the sphincter in the midline, dividing the upper half of the sphincter. The blind hind-gut is mobilized and brought down and sutured to the skin. If, however, there is only a persistent anal membrane, no mobilization is necessary and division of this membrane is all that need be done. When the hind-gut is high, it may be better to wait twenty-four hours or more to allow gas to come down to its lowest level. In this way the x-ray examination will be more accurate and will reveal the true level of the blind hind-gut. If the hind-gut is

The patient tried his best to push the sigmoid out but was not successful and the operation to date has held. However, in cases where the sigmoid has been out for some time and the viability is questionable or if recurrences take place, resection of the sigmoid and then formation of a temporary iliac anus with fixation may be the operation of choice.

Fissure is a small crack or break in the mucous membrane, due to dragging by hemorrhoids and pinching by irritable sphincter, or secondary to cryptitis (inflammation of crypts of Morgagni) or papillitis (inflammation of rectal papillae) which also produces an irritation of the sphincter and may cause a fissure by burrowing under the anal skin. For this reason the offending crypts or papillae should be removed. The lesion causes much pain, itching, and sphincteric spasm. The treatment is thorough dilatation of the sphincter, allowing the fissure a better blood supply; in intractable cases, removal of the fissure is necessary, and, in addition, the hemorrhoids should be removed.

Hemorrhoids are simply dilated veins of the rectum with fibrosis about them. They may be *external* (outside the external sphincter and arising from the inferior hemorrhoidal vein), in which case they are covered by skin, or *internal* (above the external sphincter and arising from the middle hemorrhoidal veins), or both external and internal. They cause many symptoms which are a source of discomfort to the patient. Internal hemorrhoids may cause bleeding, or, if ulcerated, they may be painful, protruding outside the sphincter on defecation. External hemorrhoids may become thrombosed, causing severe pain, or they may cause fissures and intense itching. The permanent cure is removal. Palliative treatment includes a nonresidue diet, bland suppositories, and witch hazel and anesthetic ointments for itching; for thrombosis, incision and evacuation of the clot.

Pruritus ani may be so severe and persistent as to demand more than palliative treatment. The cause may be local due to hemorrhoids, cryptitis, proctitis, enlarged papillae, fungus infection, and vaginal discharge in which it is associated with pruritis vulvae; or general due to neurasthenia, diabetes, jaundice, allergic states. The treatment in addition to local soothing application includes the treatment of the cause, and the injection of alcohol (95 per cent) is sometimes practiced. Other symptoms of anorectal disease are pain, hemorrhage, protrusion or prolapse, and discharge of pus.

Ischiorectal abscess occurs in the space named and is due to infection passing through the rectal wall into this area of loose areolar tissue. The infection may go through an infected crypt of Morgagni, a fissure, a punctured wound made by a foreign body, or, in rare cases, through a carcinomatous area. Anal ducts lined with transitional epithelium course downward from the crypts, often penetrating the internal anal sphincter, and may carry the infection into the ischiorectal space. There are fever, severe pain, especially on defecation, and, later, swelling externally. The

membrane becomes adherent and does not prolapse. In cases where there is perineal paralysis and loss of sphincter tone, the prolapse may become engorged and gangrenous and surgery may be necessary. Such cases frequently require amputation from below and suture of the mucous membrane. Great care must be exercised, however, because the prolapse may be a true one and, if so, it may permit loops of small bowel to enter into the prolapsed bowel. In the adult the prolapse of the mucous membrane is usually the result of hemorrhoids. These become thrombosed and literally pull the membrane outward after each defecation Then the mucous membrane is replaced. Such cases improve greatly after hemorrhoidectomy and are helped by sutures placed longitudinally in the mucous membrane to decrease the circumference of the bowel. Sometimes even after this procedure the mucous membrane still protrudes, and in such cases linear cauterization may be indicated.

The more troublesome type, however, is a true prolapse of the entire rectum. In true prolapse there is a hole several centimeters deep which may be felt with the finger between the anus and the prolapse. This is not present in a simple prolapse of the anal mucosa. The treatment for true prolapse consists of, first, the perineal operation and, second, the abdominal operation. Perineal operations include narrowing of the anal ring, fixation of the rectum to the sacrum or coccyx, and resection of the entire prolapse (Mikulicz operation). These operations may be employed for anal prolapse, although they are not practical for rectal prolapse, which should be handled through a laparotomy incision. In most instances the perineal type of operation for true prolapse is not indicated, and the results are not as good as those from the abdominal operation. However, if the extruded mucosa is gangrenous, it should be excised, leaving the muscle and connective tissue coats and the ends sutured together (Delorme operation). The abdominal operations are of three types: (1) obliteration of the pouch of Douglas, alone. Since the prolapse is more common in women than in men, the sagging pouch of Douglas is the offending mechanism. (2) Obliteration of the pouch with fixation of the pelvic colon. (3) Obliteration of the pouch with resection of the sigmoid flexure and temporary colostomy. We have encountered several prolapses of the rectum. One was in a man who was an inmate of the Central Hospital for the Insane. The other was a woman who was of low mental caliber. The rectal sphincters were so large and patulous that the entire hand could be introduced easily. The man was a dementia praecox and insisted on pushing the rectum out. In the woman we employed the operation of obliteration of the pouch of Douglas and in addition a ventral fixation of the uterus was done, fixing the uterus to the anterior wall of the abdomen. In the man, we obliterated the rectovesical fossa with interrupted sutures, then made a flap of the mesosigmoid, anchored the sigmoid to the psoas muscle, and then overlapped the peritoneal flap on top of the sigmoid to further anchor it. We did not do a resection nor did we do a complimentary ileostomy.

rectal carcinoma is not painful, whereas anal carcinoma is accompanied by pain. In fact, pain is usually due to anal rather than rectal disease (fissure, thrombosed or strangulated hemorrhoids, ulceration, perineal abscess, etc.) It is squamous in type as a rule but in rare instances may be basal-cell carcinoma. The lesion begins as an ulcer usually but may originate in papillomatous growths. The cancer grows rapidly and soon invades the perirectal fat or vagina and spreads by continuity. The superficial lymph nodes of the vaginal region are involved first, and later the deep nodes of this basin are involved. The hemorrhoidal venous flexures may be invaded and transport tumor cells to the liver as well as to the lungs. Treatment consists of early and complete removal by the abdominoperineal resection or colostomy with posterior resection. In late cases or those inoperable for other reasons, radium should be used. The results are almost as good as surgery.

Strictures of the rectum are caused by (1) syphilis, (2) tuberculosis, (3) new growth, (4) lymphogranuloma inguinale, (5) gonorrhea, (6) chronic ulcerative colitis, and (7) congenital defects. The symptoms are those of obstruction. Diagnosis is made by digital examination and by biopsy through the proctoscope. The treatment consists in removing the causative factor, plus repeated dilatations. Sometimes colostomy is necessary for temporary or permanent diversion of the fecal current. Resection may be necessary. See previous discussions under respective subjects.

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treatment consists of early incision and drainage as close to the anus as possible so that if a fistula results it will be short. Since it is an anatomically localized space and since it will spread around the anus, waiting invites a fistula.

Fistula in ano is a common sequel to the preceding. It is seen often in chronic ulcerative colitis and proctitis. Usually the infection descends from the anal crypt by way of the anal ducts and is carried into the surrounding tissues by way of the lymphatics. The loose fatty areolar tissue breaks down into an abscess. When it is opened or breaks, a fistula with its inner opening in an anal crypt is formed. The outer opening may be perianal, through an abscess cavity or by a direct line, or pelvirectal or retrorectal. Also, any of these potential spaces (two ischiorectals below the levators, two pelvirectal and one retrorectal above the levators) may harbor an abscess. This is an opening from the rectum to the outside which discharges pus. About 10 per cent are tuberculous and are secondary to tuberculosis elsewhere, and some are due to actinomycosis. Sometimes the fistula burrows around the sphincter in various directions. Since it is lined by epithelium, it will not heal unless it is laid open and its wall destroyed, so that granulations can form from the bottom up.

New growths may be benign (polypi) or malignant (carcinoma). The former are usually adenomas and hang in grapelike fashion from the mucosa. They are freely movable because of their pedicle, and are extruded with every act of defecation. Their relation to carcinoma has been discussed and they should therefore be removed. Their removal is easily accomplished by the cautery. *Carcinomas* may be of the soft medullary or of the hard scirrhus type. The symptoms of carcinoma of the rectum are bleeding and change in bowel habit. The diagnosis is easily made by digital and proctoscopic examination. Since internal hemorrhoids are a usual cause of bleeding, the patient is apt to ascribe the bloody stool to these. Both conditions are relatively painless at first, and valuable time may be lost. Bleeding from the rectum demands investigation by the physician. The treatment is surgical and consists of what is known as the combined abdominoperineal operation. The sigmoid is divided above the growth, and its proximal end is brought out through the left lower abdominal wall. The distal end, including the growth, is freed down to the levator ani muscles if possible; then the patient is placed in the lithotomy position, and the anus and lower rectum are freed until the entire lower bowel is removed. Variations are two-stage operations and Kraske types (removal of the sacrum and rectum from below only). Sarcoma of the colon and rectum is rarely seen. When it does occur, it is usually lymphosarcoma. Melanoma as a primary or secondary growth may occur, the former from misplaced skin elements (in the rectum) and from chromatophore cells around the anus.

Anal carcinoma occurs at the mucocutaneous border. Very few tactile corpuscles are present above the mucocutaneous junction. Therefore,

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Muscles contain about 8 mg. per 100 grams, and blood plasma 9 to 11.5 mg. per cent. Small amounts are present in the red blood cells, the lymph, the aqueous humor, and the cerebrospinal fluid. Some is found in ascitic and edema fluids.

Calcium is thus absorbed and is constantly being deposited in bone. It is also used or mobilized as needed. The level of the calcium in the blood is kept more or less constant in normal individuals through the aid of the parathyroids. McLean and Hastings state that the organism is protected against too sudden changes in the concentration of ionized calcium by the reserve supply in the blood (bound to protein) and also by the reserve in bone. *Nondiffusible* calcium is bound to serum protein. The *diffusible* calcium of the serum is in an ionized form. The calcium balance (that is, the difference between the quantity ingested and excreted) is positive (calcium retention) during growth, pregnancy, acromegaly, or after a period of calcium starvation. It is negative in infantile rickets, celiac and renal rickets, sprue, osteomalacia, hyperparathyroidism, hyperthyroidism, and starvation (calcium deficiency) and during lactation.

Fig. 322.—Osteomyelitis The dark area is the sequestrum, which has become separated and is surrounded by pus.

Bones undergo hypertrophy when subjected to strong muscular demands over long periods. Conversely, atrophy is common in disuse (immobilization for injuries, amputation stumps which are not carrying artificial limbs, paralyzed extremities). Sometimes the atrophy is out of all proportion to the disuse as in suppurative joint disease. Here it occurs early probably due to nutritional insufficiency or toxic effects. In children atrophy causes a decrease in the growth of bones both in length and thickness. In fact the skeleton like the muscles which make it work, reflect the physical efforts of the individual. Therefore the difference in skeletal development is not all a matter of heredity but in environmental requirements as well. This may be the key to the treatment of bone and joint disease.

The long bones are formed from cartilage. The *epiphysis* is the cartilaginous end of the bone where growth occurs. The shaft of the bone is called the *diaphysis*. Here growth in circumference only occurs. Adjacent to the epiphysis is the *metaphysis*, the very vascular end of the diaphysis where most infections arise. The bone is composed of a hard cortex, made of compact bone, and a loose *medulla*

Chapter 21

THE SKELETAL SYSTEM

The great mesenchymal framework of the body is necessary to house its vital organs. Nature delays the formation of the skeletal system until the later months of fetal life. Unlike the housebuilder, she forms the vital organs first, then surrounds them with the exterior. This framework has many other functions besides protection and locomotion. The bone marrow and cortex are essential to hematopoiesis, antibody formation, and calcium metabolism, whereas the muscular system, which constitutes about 40 per cent of the weight of the healthy adult body and contains 100,000 miles of capillaries, plays a vital role not only in locomotion but also in glycogen metabolism, heat regulation, circulation, antibody formation, protein metabolism, elimination of fatigue products (lactic acid), maintenance of the pH of the blood, the blood volume, water storage, etc. It may be readily seen, then, that bone and muscle constitute organs of great importance to anabolism, catabolism, and metabolic equilibrium. Health and the cure of disease are dependent in no small measure upon these organs.

BONES

The embryologial development, anatomy, and repair of bones has been described in Chapter 3. In this discussion the role of mesenchymal cells was mentioned. However, it is well to emphasize that mesenchymal cells and reticulum cells are closely related and that they give rise to bone marrow cells, fibroblasts, chondroblasts, and osteoblasts. Therefore, injuries or disease of bone may be repaired by any or all of these cells, or the cells may be transformed from one to another, even reverting back to their embryological types in some instances of neoplasia.

The chief constituent of bone is calcium. This substance must be ingested in sufficient amount, absorbed, and metabolized and must reach the skeleton in order to maintain positive calcium balance. Furthermore, it must not be dissipated faster than it can be assimilated in order that a positive balance may persist.

Bone calcium exists as calcium carbonate and tricalcium phosphate. Other minerals present in small quantities are phosphorus, magnesium, potassium, sodium, chlorine, fluorine, and iron. Organic matter in bone (aside from marrow) is chiefly protein, ossein with small amounts of osseomucoid, and albuminoid.

Calcium is needed in (1) coagulation of blood, (2) formation of bone, (3) cardiac rhythmicity, (4) maintenance of neuromuscular excitability, (5) milk production, and (6) membrane permeability.

Calcium is present in the ingested food in organic and inorganic forms. It is absorbed in the small intestine and is excreted into the colon through the bowel wall and, in small amounts, in the urine. Calcium constitutes about 2 per cent of the weight of the adult body, and 97 per cent of the total quantity is contained in the skeleton.

Outline of Bone Diseases

A. Congenital anomalies
B. Injuries
   1. Fractures
C. Diseases of bone due to defective mesenchymal framework
   1. Osteogenesis imperfecta
   2. Achondroplasia
   3. Fibrous dysplasia
D. Infections and inflammations of bone
   1. Osteomyelitis
   2. Syphilitic osteitis
   3. Tuberculous osteitis
   4. Pulmonary osteoarthropathy (?)
   5. Echinococcus cyst
   6. Eosinophilic granuloma
E. Circulatory disorders of bone (epiphysitis)
   1. Legg-Perthes' disease
   2. Osgood Schlatter's disease
   3. Köhler's disease
   4. Freiberg's infraction
   5. Scurvy (vitamin C deficiency)
F. Defective assimilation or utilization of calcium due to vitamin D deficiency
   1. Rickets (in children)
   2. Osteomalacia (in adults)
G. Diseases of bone due to hyperparathyroidism
   1. Osteitis fibrosa cystica (von Recklinghausen's disease of bone)
   2. Paget's disease of bone
H. Changes due to excessive excretion of calcium (osteoporosis)
   1. Cushing's disease
   2. Hyperthyroidism
   3. Diabetes
I. Neoplasms of bone
   1. Metastatic growths
   2. Multiple myeloma
   3. Hand-Schüller-Christian's disease (xanthomatosis)—lipoid storage diseases
   4. Multiple chondral exostosis and osteoma, hemangioma, neurofibroma
   5. Osteogenic sarcoma
   6. Benign giant-cell tumor
   7. Unicamerate cyst
   8. Adamantinoma, liposarcoma, lymphoblastoma, hemangioendothelioma, hemangiosarcoma, fibrosarcoma, chondrosarcoma
J. Disorders of the vertebral column
   1. Injuries
   2. Infections (tuberculous spondylitis)
   3. New growths

Congenital Anomalies of Bones and Joints

Deformities of the skeleton may occur in the earliest embryonic stage or may be due to intrauterine constrictions, amputations, or interference with development in other ways. The following is a list of some of the more common anomalies: congenital clubfeet (talipes equinovarus), adduction of forefoot (metatarsus varus), eversion and dorsiflex-

(marrow), made of cancellous bone. Surrounding the cortex is a thin osteogenetic membrane in two layers known as the *periosteum*. Its outer layer carries the blood and nerve supply, while its inner layer is filled with osteoblasts. Lining the cancellous bone is another membrane, the *endosteum*, filled with bone-forming cells. Since bone is formed on a connective tissue framework, its calcium deposits occur along trabeculae and in lamellar fashion. These are seen in all directions and surround the Haversian canals which carry blood into the compact bone and medulla (Haversian lamellae). The principal artery to a long bone in the upper extremity runs toward the elbow; in the lower extremity, away from the knee. Flat bones are formed directly from membrane and are called membranous bones. They heal with connective tissue. In the skull the diploe corresponds to the marrow cavity.

Fig. 323.—Extensive chronic osteomyelitis of the humerus. The x-ray picture shows the sequestrum, which occupies the entire shaft partially surrounded by involucrum.

In the diagnosis and treatment of injuries and diseases of bones, it must be remembered that muscles, tendons, and ligaments are attached to the bones and that between the bones are the joints, which make locomotion possible. If a bone deviates from its normal weight-bearing or stress direction, all other bones and joints along this line of force may be affected (Wolff's law), although there is a tendency on the part of nature to correct deformities insofar as possible to prevent changes in stress upon joints.

rhage, or through nerves, severing them. Should a fragment break through the skin, a simple fracture would be converted into a compound one. For immobilization, any board or hard cardboard will do. A few rules to follow are:

1. Pad the splint well with cotton, cloth, or pillows.
2. Extend the splint above and below adjacent joints.
3. Tie the splint tight. This is absolutely necessary to prevent movement of the fragments and to alleviate suffering. A loose splint is worse than none at all.
4. Two splints (anterior and posterior) are better than one.

Fig. 325.—Garré's sclerosing osteomyelitis. The low power shows the involvement of compact and cancellous bone. The high power shows the absence of suppuration, much connective tissue, and many lymphocytes. The large cells seen in the upper right section are osteoblasts.

Fractures are usually due to external violence or strong muscular action. However, pathological fractures occur in diseased bone with very little exciting cause.

The treatment of fractures is designed to obtain good union of the fragments in a good functional position. The restoration of movements in joints and power in the muscles is desired in the shortest possible time. Some general observations in the treatment of fractures are as follows: (1) The earlier the reduction of the fracture, the easier and safer, and better the result. (2) Anesthesia is necessary—general in children and in adults with extensive fractures where the condition permits; local in less extensive fractures in adults. (3) Closed reduction is preferable to open reduction if possible. Traction is advisable in severe

ion of ankle (talipes calcaneovalgus), flat feet (pes planus or valgus), imperfectly formed limbs (ectromelia), extra digits (polydactylism), webbed fingers and toes (syndactylism), overgrowth of digits (macrodactylism), clubhand (manus vara), radioulnar synostosis, asymmetrical development (hemihypertrophy, hemimacrosomia), partial fibrous ankylosis of many joints (arthrogryposis multiplex congenita, amyoplasia congenita), absence of part or all or both clavicles with increased diameter of cranium and abnormal dentition (cleidocranial dysostosis), elevation of the scapula (Sprengel's deformity), congenital synostosis of the cervical spine (Klippel-Feil syndrome), congenital dislocation of the hip, knee, patella, ankle, shoulder, elbow, wrist, congenital absence of the radius, tibia, or fibula, progressive dislocation of the radioulnar joint (*Madelung's deformity*), *acute angling of femoral neck* (*congenital coxa vara*), obtuse angling of the neck of femur (congenital coxa valga). Treatment should be in early infancy and consists of mechanical appliances or surgical maneuvers, depending on the type encountered.

Fig. 324.—Chronic osteomyelitis with draining sinus. The low power shows the skin densely adherent to the bone, and the epithelium-lined sinus tract. The high power reveals the extent of epithelial penetration. To cure the sinus, all of the epithelial lining must be removed.

Fractures

The repair of bone is discussed in Chapter 3. In bone injuries, as in other injuries, bleeding, if present, must be controlled first. Then the patient is treated for shock (see Chapter 14). *A patient should not be moved until the fractured part is immobilized.* If this is not done, the broken bone may tear through blood vessels, starting a severe hemor-

rhage, or through nerves, severing them. Should a fragment break through the skin, a simple fracture would be converted into a compound one. For immobilization, any board or hard cardboard will do. A few rules to follow are:

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compound fractures and in oblique and comminuted fractures of the shafts of long bones, especially the humerus and femur, where thick muscles cover the bone and maintenance of reduction is difficult to maintain. Open operation is done when reduction or maintenance cannot be secured by other methods; also in cases where large lengths of bone have been devitalized and bone graft is necessary. (4) Immobilization is secured by recumbency, bandages, slings, traction, splints, plaster of Paris, wires (Kirschner), pins, screws, nails, flanged nails, bands (Parham), plates (Sherman), ivory pegs, plates, and bone. Unabsorbable foreign bodies in fractures, like the same material in soft tissue wounds, should not be used in contaminated or potentially contaminated fractures (compound fractures, badly contused wounds, hematoma of large size, etc.).

Fig. 326.—Tuberculosis of the wrist. There are generalized osteoporosis and disintegration of the joint as well as bone destruction.

Infection is more apt to occur, and the foreign body will have to be removed or will slough out due to osteomyelitis. Immobilization should be maintained with the finest material possible. The porosity of the bone and its size and position will be determining factors. However, large heavy spikes, bands which encircle bones, and plates which produce ischemia all interfere with blood supply and therefore will delay healing (see Chapter 3). (5) The general condition of the patient is important in obtaining good healing and good function; therefore, any form of immobilization which will allow early movement of the patient as a whole is desirable. This is especially true in the aged. (6) Compound

fractures are treated as open contaminated wounds (see Chapter 16) and are débrided and then immobilized and protected by chemotherapeutic agents and antibiotics.

Diseases of Bone Due to Defective Mesenchymal Framework

Osteogenesis imperfecta, also called *fragilitas ossium* and *osteopsathyrosis*, is congenital in origin and consists of an atrophic, brittle type of bone which gives rise to multiple fractures early in life. They heal slowly. The child may outgrow the condition. Vitamins D and K in early life help.

Achondroplasia is another congenital bone defect consisting of a failure of the epiphyseal cartilage to ossify. Longitudinal growth is interrupted and the child fails to grow, becoming a dwarf.

Fibrous dysplasia is also called fibrosa cystica disseminata, osteodystrophia fibrosa, fibrocystic disease of bone, and Albright's disease. It may involve one or many bones. The cortex is expanded and thin over the defects in the bone. These areas are filled with gelatinous grayish-white tissue, which contains thin-walled capillaries, foreign body giant cells, trabeculae of new bone, hyaline cartilage, and some nests of foam cells. The symptoms are swelling and pain. Very often a pathological fracture is the first symptom. Blood calcium and phosphorus are normal. In early life the disease is accompanied by pigmentation of the skin, precocity in females, premature skeletal growth, abnormalities of the heart and kidneys, and multiple lesions and deformities of bones (Albright's disease). Treatment consists of curettage of the bone defects and filling in with bone chips. If polyostotic, this must be done in stages.

Infections and Inflammations

Infections in bone are not as common as in the era before antibiotics and chemotherapeutic agents. In fact, acute hematogenous osteomyelitis is now extremely rare. Or, if it does occur, then penicillin and the sulfonamides used in the treatment of the primary conditions eradicate the bone infection before recognizable destruction occurs. Nongranulomatous inflammations are hematogenous and exogenous osteomyelitis, Brodie's abscess, and echinococcus cyst. Granulomatous lesions are syphilis, tuberculosis, eosinophilic granuloma, coccidioidal granulomas, Boeck's sarcoid, actinomycosis, blastomycosis, leprosy, and granuloma inguinale.

Osteomyelitis is an infection of the medulla of bone which spreads through the cortex and medulla, sometimes causing widespread destruction. Its cause is usually hematogenous, although in adults it usually occurs as a result of direct trauma such as compound fracture or infection following the use of bands or plates. A child may have a series of boils or otitis media, and bacteria from the acute focus may be carried to the metaphysis of a bone. Trauma may influence the site affected.

The mechanism of infection has been studied extensively. Cultures of staphylococci which are injected into bone through a drill hole fail to produce osteomyelitis unless under pressure. Sterile water injected under pressure produces necrosis but no infection (compact bone and can-

Fig. 327.—*A*. Legg-Perthes disease (osteochondritis *deformans juvenilis*). *Note the fragmentation of the head of the femur*, and the shortening and broadening of the neck on the left side. *B*. Osgood-Schlatter disease, showing the fragmentation of the epiphyses of the tibial tuberosities.

cellous bone in the metaphysis are normally sterile). Staphylococci injected into the nutrient artery of a bone in experimental animals do not produce osteomyelitis. If acacia or sodium morrhuate is added, or if the culture is injected under great pressure, osteomyelitis develops. Some experimenters have produced the disease in animals following the intra-

Fig. 329.—*A*. Rickets. X-ray showing the beading at the costochondral junction (rachitic rosary). *B*. Coxa vara deformity on the left. *C*. X-ray showing the irregularity and cupping of the epiphyseal lines.

venous injection of *Staphylococcus aureus*. The experimental work, though conflicting, tends to establish the same laws of infection in bone as elsewhere; *namely*, if the local resistance of the metaphysis is decreased by local factors (trauma, deficient blood supply) *or by general disease* (septicemia, avitaminosis), infection occurs when bacteria are injected locally or systemically.

The compact or cortical bone is almost absent at the metaphysis. The adult is not susceptible to hematogenous osteomyelitis because when the epiphysis becomes ossified and fuses, the metaphysis has a more adequate blood supply (being supplied by the epiphyseal, juxtaepiphyseal, periosteal, and nutrient arteries).

Fig. 329.—Osteomalacia. There is decalcification of the vertebrae and the pelvic bones. *The vertebral bodies appear as mere outlines.* The patient is a woman aged 61 years. The complaint was "general pains in legs and abdomen." Physical examination and all laboratory tests normal.

An interesting clinical observation is the rarity of involvement of other organs and tissues in multiple osteomyelitis unless a general bacteriemia is present. Better stated, the spread of the infection from the acute focus seems to *be limited to bones. Various explanations* of this have been suggested: (1) the relatively few macrophages present in the cancellous bone of the metaphysis, which make the local resistance poor;

(2) the slow circulation in the metaphysis due to the many capillaries; (3) the many end arterial twigs; (4) the small size of the capillaries which results in the trapping of the organisms (in the lung, for example, they are larger, permitting the organism to go through and become engulfed by septal or dust cells).

The infection causes destruction of bone and, if unchecked, may burrow through the cortex and strip the periosteum as well as the endosteum. This gives rise to a necrotic piece of bone called a *sequestrum*. Around this, nature forms a sheath of new bone, the *involucrum*. Pus works its way out of a necrotic hole in the cortex (cloaca) which permits draining sinuses to occur in the skin. The early symptoms and

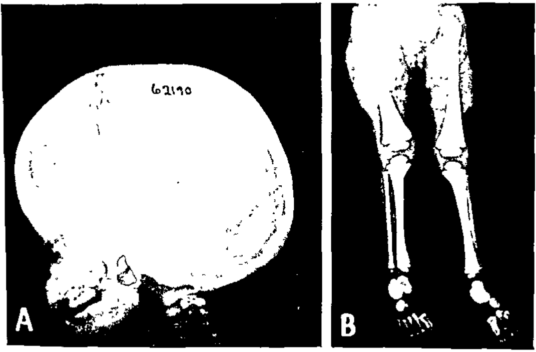

Fig. 330.—*A*. Marble bones (Albers-Schönberg disease). There is increased density of the bones of the base of the skull. *B*. Marble bones of the lower skeleton. Note the chalky appearance of the bones. The disease is also called osteosclerosis fragilis. Pathologic fractures are common.

signs are severe pain and tenderness over the affected bone near the epiphyseal line, high fever and leucocytosis (the result of pus under pressure), great prostration, and, in infants, convulsions. The diagnosis is not always easy because *x-ray does not help in the early stages.* The history, clinical symptoms and signs, and exploratory trephining establish the diagnosis.

The treatment consists of large doses of penicillin with sulfadiazine and rest in bed unless a subcutaneous abscess forms, then incision and drainage. Sequestra are extremely rare now, especially in very young children. This is due to the fact that the thin porous cortex surrounding the metaphysis allows exit of the pus. In older children and adults

the same treatment is now employed by most surgeons: rest in bed and immobilization of the affected leg until localization occurs; then simple drainage of the localized abscess. Exploratory trephining is no longer practiced. Late and neglected cases with sequestration require a "gutter" operation on the bone, with removal of sequestra (sequestrectomy), followed by infrequent dressings to allow the cavity to heal from the bottom up. The affected leg is immobilized for protection against fracture and to encourage healing.

The treatment of chronic osteomyelitis differs little from the treatment of an abscess elsewhere and may be dogmatically outlined as follows:

1. *Wait for localization* (complete separation of the sequestrum).

2. Provide ample drainage (a long gutter should be made over the involved area, through the involucrum).

3. Remove all dead bone gently and carefully but not healthy granulation tissue.

4. Obliterate the dead space. (The area will then fill in with granulation tissue, which is changed to osteoid tissue and bone.)

5. Secure rest to the part by cast or splint.

6. Change the dressing infrequently just as in the case of other wounds. The Orr treatment consists of packing the cavity with petrolatum gauze, putting on a cast, and letting the bone severely alone for six to eight weeks. Results have been good. Open casts, with occasional irrigations with normal saline, eliminate the absorption of toxic products and are used by many surgeons.

Maggot therapy is used by some to aid in "cleaning up" the cavity. Others use allantoin, which is thought to be the healing substance supplied by the maggots. Pectin-agar mixtures, as described by Haynes and co-workers, have given good results.

7. Give attention to the general care of the patient. This includes rest, attention to water balance, and blood transfusion.

8. Staphylococcic toxoid or vaccine still have advocates in the treatment of chronic lesions. Usually this is unnecessary if all sequestra have been removed.

Brodie's abscess is an illustration of a so-called nonspecific infection which behaves clinically like tuberculosis. It is caused usually by the same organisms as acute hematogenous osteomyelitis but is very insidious in onset. The center of the abscess is filled with granulation tissue which later changes in part to connective tissue with the formation of pockets and cysts filled with serous or purulent material. The treatment consists of wide open drainage and saucerization to allow for healing from the bottom up.

Echinococcus cysts occasionally occur in bone and are discovered by x-ray examination. The patient may feel a tumor, or soft tissues may

be involved due to leakage. The lesion is polycystic and sharply defined. Treatment consists of excision and marsupialization.

Syphilitic Osteitis.—The "aching bones" of persons with syphilis were known to the early physicians. The bone involvement in secondary syphilis is a *periostitis;* in tertiary syphilis, *hyperostosis* ("saber tibia") and *necrosis,* due to gumma. The x-ray and serological tests, together with the history and general symptoms, confirm the diagnosis. The treat-

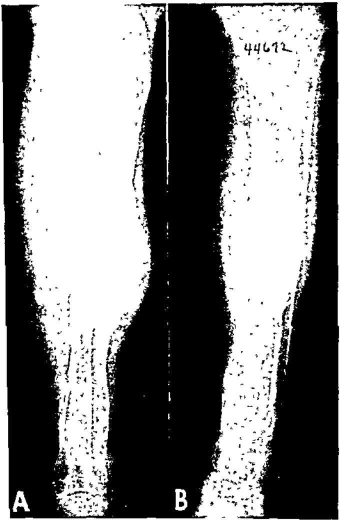

Fig. 331.—Osteitis fibrosa cystica (von Recklinghausen's disease). This was due to a parathyroid adenoma, with hyperparathyroidism. *A.* Lateral view. *B.* Anteroposterior view.

ment is limited to antisyphilitic treatment, including large doses of penicillin unless sequestration takes place. This demands the removal of the dead bone (sequestrectomy). (Chapter 9.)

Tuberculous Osteitis.—Tuberculosis of bones is an important problem since it usually affects children. The behavior of tuberculosis in bone is similar to its behavior elsewhere: There are destruction of bone,

caseation, *and cold abscess formation. The bacillus lodges in the metaphysis* and extends into the epiphyseal cartilage, frequently involving the joint. Tuberculosis infects bone through the blood stream or by way of contiguous joints. *It is almost impossible to induce tuberculosis in a* bone by injecting tubercle bacilli either into the blood stream or directly into the bone. If previous tuberculosis has been present, a gelatinous de*generation, with fibromyxomatous change, occurs, making the bones sus*ceptible *because of a tuberculous endarteritis of the nutrient and metaphyseal vessels.* The diaphysis of a bone is occasionally affected, especially *in small bones* (tuberculous dactylitis), *due to the fact that the* small vessels break up immediately upon entering the bone. Tuberculosis in a long bone is due to a tuberculous endarteritis of the nutrient artery *at its entrance.*

Fig. 332.—Multiple myeloma of bone. Note the punched-out appearance of the areas in the skull. Other portions of the skeleton were similarly affected.

The epiphysis may be involved (1) from the metaphysis, (2) directly, *from the joint, or* (3) *indirectly, if the synovial* membrane is related to the epiphysis without extending to the diaphysis. *Diagnosis is made from* a history of a slowly evolved, "cold" process, "night cries" due to muscular *contraction of the spastic muscles,* a positive von Pirquet test, evidence of tuberculosis elsewhere, and characteristic x-ray findings. The treatment consists of immobilization and the general treatment *of the* disease. Ultraviolet light and sunshine aid in the arrestment. Streptomycin is extremely *valuable. In adults* fusion or surgical fixation of the involved joint is indicated (arthrodesis, spinal fusion).

Pulmonary osteoarthropathy (acropachy) is a thickening of the distal phalanges of the hands and feet, nonpitting edema of the distal portions of the extremities and subperiosteal proliferation of the bones of the arms and legs, rarely synovitis of the joints associated with chronic pulmonary or cardiac disease (lung abscess, chronic empyema, tuberculosis, congenital and valvular heart disease). The fingers become clubbed and the nails curve. The cause is unknown, although the associated cyanosis makes one think of a vascular as well as a nutritional (and perhaps infectious) process. Great improvement follows the eradication of the chronic focus.

Eosinophilic granuloma is probably not due to an infection, virus or bacterial. It is a granulomatous lesion causing destruction of one or more bones usually in young males. Some observers state that it is related to Hand-Schüller-Christian disease or to Letterer-Siwe disease

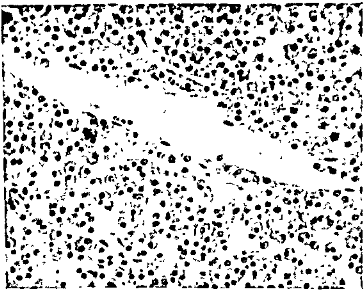

Fig. 333.—Plasma-cell myeloma of bone Note invasion of cells into the blood vessel This permits widespread dissemination.

(generalized reticulo-endothelial disease occurring in infants and rapidly fatal). The symptoms and signs are those of infection: fever, leucocytosis, anorexia, and malaise, and, locally, pain, swelling, and tenderness. Pathological studies of the tissue early show necrosis and hemorrhage with various cells (eosinophils, neutrophils, lymphocytes, plasma cells, foreign body giant cells); later the predominating cells are the round or polyhedral foam cells with small nuclei and reticulated cytoplasm. Diagnosis is made by the x-ray and biopsy. Treatment consists of excision.

Circulatory Disorders of Bone

In growing children the epiphysis may become inflamed due to some local circulatory disturbance, brought on often by a trifling injury

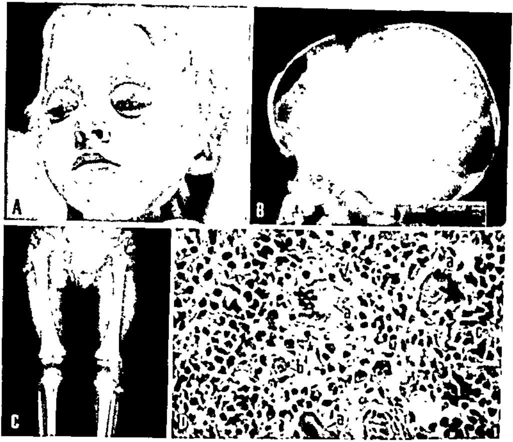

Fig. 334.—Hand-Schüller-Christian's disease. *A.* Clinical photograph of a 6-year-old child with Hand-Schüller-Christian's disease. He is pale and emaciated with bilateral exophthalmos, an enlarged skull, soft, bulging swelling beside the right ear, and bilateral choked discs. The child's father stated that he had been drinking three gallons of water a day and that he had passed "enormous" quantities of urine. *B.* Lateral x-ray photograph of the skull. The lateral examination of the skull shows a sharply circumscribed defect in the right frontal bone and several smaller defects of a similar type in the parietal region. One of the characteristic findings in lesions of this type (xanthomatosis) is the absence of any sclerotic reaction at the margins of the sharply circumscribed lesions. *C.* Examination of the long bones of the lower extremities shows areas of decreased density in the upper ends of the femurs, more numerous on the right, and a single lesion in the upper end of the left tibia. These lesions are typical of those seen in Hand-Schüller-Christian's disease. *D.* High-power photomicrograph of tissue taken from the area of defect in the previous case showing the usual findings of Hand-Schüller-Christian's disease (xanthomatosis of bone). *a,* Giant cells, some of which show fatty vacuoles in cytoplasm (fat stains show a large amount of lipoid usually thought to be cholesterol in this particular tissue); *b,* cells containing large granules of hemoglobin pigment; *c,* large mononuclear and epithelioid cells. Eosinophiles which are often seen in these cases are not plain enough in this picture to be identified.

Hand-Schüller-Christian's disease belongs to the group known as lipoidoses. It is also known as generalized visceral xanthomatosis. The usual characteristics of the disease are unilateral exophthalmos, diabetes insipidus, retarded development and defects in the bones, chiefly the skull, pelvic girdle, and the vertebrae.

Abnormal lipoids, chiefly cholesterol esters, accumulate in the cells of the reticulo-endothelial system. X-ray therapy over the affected bones is efficacious. However, relapses are common. The other two diseases which belong in this group and which show an enlarged spleen are (1) Gaucher's disease (which is also known as essential lipoid histiocytosis, cerebroside lipoidosis, and large cell splenomegaly), which will be discussed in Chapter 22, and (2) Niemann-Pick disease (also known as lipoid histiocytosis, phosphatide lipoidosis), which is characterized by splenomegaly, hepatomegaly, retarded development, emaciation, gastrointestinal symptoms, and lymphocytosis. Gaucher's disease and Niemann-Pick disease are usually fatal.

Hand-Schüller-Christian's snydrome offers a more favorable prognosis. The latter is the only one of the three that shows characteristic bone changes. This patient was improved by x-ray therapy. However, he returned later in a state of coma. He had mumps at this time. He recovered from this and was released from the hospital greatly improved.

(epiphysitis, osteochondritis, subchondral necrosis, aseptic necrosis). This causes pain and deformity of the part, somewhat resembling the effects of tuberculosis. In the hip, a flattened femoral head occurs. This is known as Legg-Perthes' disease. Inflammation of the tibial tubercle epiphysis gives rise to Osgood-Schlatter's disease; of the tarsal scaphoid, to Köhler's disease; of the second metatarsal head, to Freiberg's infraction. Other bones which may be involved are vertebral bodies, femur, patella, astrogalus, clavicle, humerus, radius, ulna, iliac crests, symphysis pubis. Diagnosis is made by x-ray and by ruling out tuberculosis. The part is immobilized and protected from injury, with resulting cure and perhaps some deformity.

In *scurvy,* while the bone is not directly affected, hemorrhages occur beneath the periosteum, giving rise to bone pain. The disease is caused by lack of vitamin C (ascorbic, or cevitamic, acid), the vitamin which preserves the normal consistency of the intercellular ground substance of various tissues (notably the dentine of the teeth, connective tissue, and the capillary endothelium). The first symptom of scurvy in children is irritability; in adults, various psychoses. The treatment is administration of vitamin C, either in the diet (citrus fruits) or as cevitamic acid.

Diseases Due to Deficiencies of Calcium or Vitamin D

Rickets.—Vitamin D, which occurs in cod-liver oil and is synthesized by sunshine in the body, aids in the assimilation and utilization of calcium. In children its absence or deficiency gives rise to *rickets (rachitis).* The disease appears between the sixth and eighteenth months of life and is characterized by a bony softening, with enlarged epiphyses, deformity of the skull ("square head"), delayed dentition, bowlegs or knock-knees, "pigeon" breast, and enlarged costochondral articulations ("rachitic rosary"). Sunshine, proper diet (mother's milk in infancy, if possible), and cod-liver oil prevent it. Cod-liver oil cures the disease but bony changes may persist.

Osteomalacia occurs in adults—usually in pregnant women, though it may occur in any undernourished person. It is due to lack of mineral salts or deficiency of Vitamin D and in its pathology resembles rickets. The treatment is good and proper food, sunshine, and cod-liver oil.

Diseases of Bone Due to Hyperparathyroidism

We shall learn in Chapter 23 that the parathyroids are intimately related to calcium metabolism. As a result of an adenoma or more obscure causes, the parathyroids may secrete an excess of their hormone. This causes decalcification of bone, hypercalcemia, and excessive excretion of calcium in the urine, with, perhaps, a formation of renal calculi. There may result multiple bone cysts throughout the skeleton, *osteitis fibrosa cystica* (von Recklinghausen's disease). The disease is diagnosed

by x-ray examination, and attention is often first called to it by a pathological fracture. Added to this, the high blood calcium with low blood phosphorus and other symptoms establish the diagnosis. Single cysts are probably not related to parathyroid disease. In the aged, Paget's disease, or osteitis deformans, causes softening and overgrowth of bone, bowing of the extremities, and enlargement of the head. The disease is rare and thought to be related to parathyroid dysfunction. Sarcoma may be a complication of this disease.

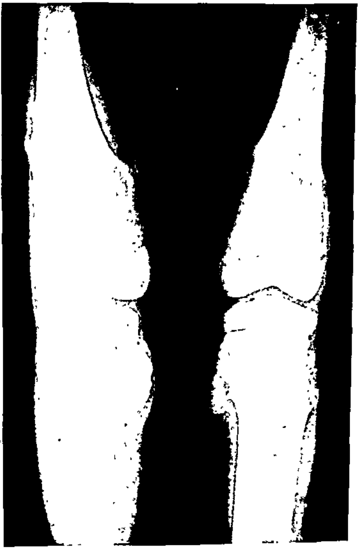

Fig. 335.—Multiple exostoses of the femur, tibia, and fibula (benign). Anteroposterior and lateral views.

Osteoporosis is not a disease, and it is not a disorder of calcium metabolism. It is a deficiency in laying down of osteoid tissue. It is a generalized atrophy of bone matrix when prolonged immobilization has produced bone atrophy.

Adult bone is continually being formed and resorbed. Bone may be deficient because resorption is too great (hyperparathyroidism with

Fig. 336.—Osteochondroma of the femur (benign)

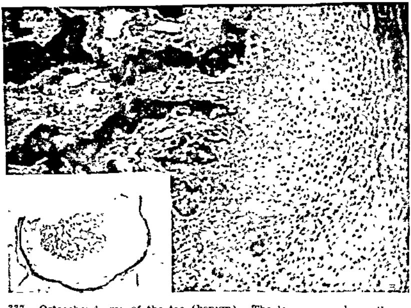

Fig 337—Osteochondroma of the toe (benign). The low power shows the cancellous bone capped by cartilage which in turn is covered with skin; the high power, cancellous bone on the left and cartilage on the right.

osteitis fibrosa cystica generalisata) or because formation is too little (osteoporosis or osteomalacia). If the osteoblasts do not lay down sufficient matrix or osteoid tissue, there is osteoporosis. If, however, the matrix is laid down but not calcified, there is rickets or osteomalacia. Factors which may be responsible for osteoporosis are disuse, dietary deficiency, gastric hypoacidity, repeated pregnancies, senescence, postmenopausal period. Also, in Cushing's disease, hyperthyroidism, and diabetes, a thinning of bone is seen. Control of the underlying disorder results in redeposition of matrix and calcium. Fractures are apt to occur in these brittle bones.

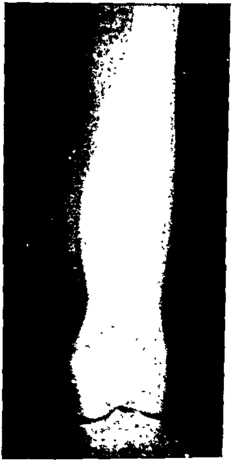

Fig. 338.—Osteogenic sarcoma of the femur. The shaft is broadened due to bone production. This is the periosteal type (osteogenetic).

Sudeck's atrophy (posttraumatic painful dystrophy of the extremities, acute atrophy of bone, posttraumatic osteoporosis, traumatic angiospasm, chronic traumatic edema, peripheral trophoneurosis, reflex nervous dystrophy) has been discussed in Chapter 6. The osteoporosis is a late phenomenon and probably results from a combination of factors; namely, disuse and deficient blood supply. It is greatly improved by sympathetic ganglionectomy, neuropsychiatric treatment, and mobilization.

Neoplasms of Bone

Neoplasms of bone are many and varied. Ewing's classification of sarcoma of bone and bone marrow is given in Table XXIV.

TABLE XXIV

EWING'S CLASSIFICATION OF SARCOMA OF BONE AND BONE MARROW

MALIGNANT	BENIGN
I. Osteogenic series	
Osteogenic sarcoma	
1. Medullary and subperiosteal	1. Exostosis
2. Telangiectatic	2. Osteoma
3. Sclerosing	
4. Periosteal	
5. Fibrosarcoma	
(a) Medullary	
(b) Periosteal	
6. Parosteal, capsular	
II. Chondroma series	
1. Chondrosarcoma	1. Chondroma
2. Myxosarcoma	
III. Giant-cell tumor series	
1. Malignant	1. Epiphyseal giant cell tumor
IV. Angioma series—Ewing's tumor	
1. Angioendothelioma	1. Cavernous angioma
2. Diffuse endothelioma	2. Plexiform angioma
V. Myeloma series	
1. Plasma cell—plasmacytoma	
2. Myelocytoma	
3. Erythroblastoma	
4. Lymphocytoma	
VI. Reticulum-cell lymphosarcoma	
VII. Liposarcoma	

Secondary Bone Tumors.—Secondary tumors of bone are common, especially when the primary carcinoma is in the breast, prostate, ovaries, kidney, and adrenal and thyroid glands. Thus cancer of the breast may invade the spine where it may cause a collapse of the vertebra; also the ribs, sternum, humarus and, rarely, the upper femur. The prostate usually is responsible for metastases to the pelvic bones and lower spine. Any bone may be involved, and the reaction in the bone is not always osteolytic. At times there is increased density around the metastatic area, and rarely osteogenesis is stimulated. Treatment is that of the primary lesion and x-ray therapy to the bones which are involved. In addition, castration and stilbestrol cause amelioration of bone lesions in carcinoma of the prostate (see Chapter 23). Testosterone proprionate alleviates pain in metastatic cancer from breast and ovaries but does not materially change the bone picture (see Chapter 16). Radioactive iodine may be used to discover early thyroid metastases (with the aid of the Geiger counter) and to cause recession in the bone and thyroid lesion (see Chapter 22). Radioactive phosphorus and other elements may prove helpful in other forms of metastatic cancer.

Primary Bone Tumors.—*Multiple myeloma* is a fatal disease in adults, consisting of an infiltration of bones, usually with plasma cells. Soft tissue

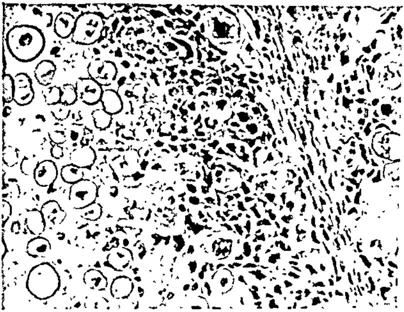

Fig. 339.—Osteogenic sarcoma. On the left are chondroblasts; in the center, tumor cells, and on the extreme right, osteoid tissue. The tumor cells are polyhedral and spindle-shaped. A few malignant giant cells are seen.

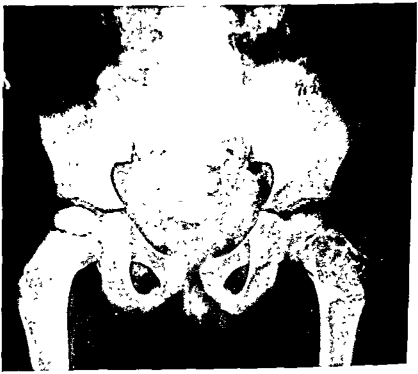

Fig. 340.—X-ray photograph of benign giant-cell tumor of the femur, showing expansion of the bone, with thinning of the cortex.

Fig. 341.—Benign giant-cell tumor of the clavicle. The giant cells are seen to arise from the capillary endothelium. There is no bone production. The fibrous stroma, filled with spindle-shaped cells, makes up the bulk of the tumor.

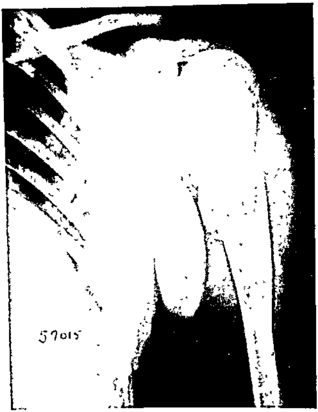

Fig. 342.—Pathologic fracture of the humerus directly through a bone cyst. Note thinning of bone and cystic appearance.

Fig. 343.—Adamantinoma. J. G., a woman aged 52 years, was admitted to the hospital complaining of a draining sinus in the left gingiva. This was in 1932. In 1933 a cyst was curetted from the left mandible. She had subsequent recurrences at frequent intervals and in 1937 took x-ray treatment over a period of four years consisting of treatments approximately once a month. In 1940 she came to the hospital with a tumor mass measuring approximately 3 by 4 inches. At this time she had severe pain in the left mandibular area and an operation was deemed advisable. Accordingly, a hemiresection of the mandible was done on the left side. The external carotid artery was ligated first, and then the entire left mandible was removed together with the submaxillary gland and the lymph nodes in the left anterior triangle of the neck. The growth proved to be an adamantinoma.

The patient came back to the hospital in July, 1949, for treatment for hypertension. At this time it was found that there was no recurrence and that the right half of the mandible was functioning in a satisfactory manner. *A*, Clinical photograph of the woman as she appeared in July, 1949. *B*, Photograph of the gross specimen showing the lesion and *C*, Longitudinal section of the mandible and its tumor mass. It will be noted that the growth is partially solid and partially cystic. *D*, Low-power photomicrograph. Note layer of columnar cells (enameloblasts) at periphery and loose stroma in the interior of irregular tumor masses. (Specimen prepared by Dr. Harold C. Thornton, pathologist.)

metastases occur. Sometimes plasma cell leucemia is the terminal picture with 30,000 to 40,000 cells per cubic millimeter. Diagnosis is made by x-ray examination, together with the occurrence of Bence Jones protein in the urine, which is present in about 50 per cent of the cases, and biopsy. The treatment is by x-ray which may temporarily alleviate but will not cure this disease. *Lipoid storage diseases of bone include xanthomatosis* (Hand-Schüller-Christian disease), Niemann-Pick's disease, and Gaucher's disease (see Chapters 16 and 22). *Xanthomatosis* causes a thinning of bones in children due to the deposit of fat cells. X-ray examination and the finding of an increase in the blood cholesterol and biopsy make the diagnosis. Restriction of fat in the diet and x-ray treatment may bring about its remission. In Gaucher's disease splenectomy may help. *Multiple chondral exostosis* and *osteoma* are benign cartilaginous and bony tumors, often congenital in origin. They occur near the epiphysis or the adductor tubercle and under the big toenail (subungual). Diagnosis is made by x-ray. The treatment consists of removal.

Fig. 344.—Endothelial myeloma of bone (Ewing's tumor). There is a monotonous appearance of large cells with ovoid nuclei and scanty protoplasm. Broad bands of connective tissue traverse the masses of cells.

Multiple cartilaginous exostosis (hereditary multiple exostosis; diaphyseal aclasis, hereditary deforming chondrodysplasia, and dyschondroplasia) is also a disease of benign, bony, and cartilaginous growths which are multiple, bilateral, or symmetrical and may involve any bone in the body except the membranous bones and the tarsal and carpal bones. The lesions are common at the epiphyseal end in the cartilaginous plates. Treatment is indicated if the lesions interfere with function. Chondrosarcoma sometimes occurs.

Hemangiomas are benign growths which may affect the vertebra, skull, pelvis, or long bones. They may cause pain and deformity. Diagnosis is made by x-ray. Treatment consists of excision.

Neurofibromatosis of bone occurs rarely and may arise from nerve fibers in the periosteum, cortex, or medulla. If near the epiphysis, they may stimulate or retard growth. Pseudoarthrosis, spontaneous fractures, and scoliosis may result from their presence. They should be removed.

Osteogenic sarcoma, as its name implies, arises in bone. Some authors use the term to include osteosarcoma, chondrosarcoma, and fibrosarcoma of bone. It may be osteogenetic (bone-forming) or osteolytic (bone-destroying). It may be very malignant, the latter variety more than the former. It usually occurs in children or young adults. Osteosarcoma is a term used to denote a primary osseous tumor arising from osteoblasts or their forebears. Osteoblastic osteosarcoma usually arises from the diaphyseal periosteum. Osteolytic osteosarcoma arises in the metaphyseal medulla and has been called a malignant bone aneurysm or cyst.

Fig. 345.—Clinical photograph (J. B.) showing large carcinoma of right hand. There had been previous attempts at removal. Axillary metastases were present. The entire upper extremity was removed by the interscapulothoracic *disarticulation technique* described in Figs 340, 341, 342, 343, and 344. (From Berman, J. K., Surgery 18: 256, 1945)

Osteosarcoma spreads by direct extension and by the blood stream. Diagnosis is made by x-ray and by biopsy, with tourniquet immediately proximal to the growth. Amputation is done if the condition is diagnosed early. This may necessitate disarticulation of an extremity or the entire extremity and its attachments: in the arm, interscapulothoracic disarticulation, and in the leg, hemipelvectomy, exarticulation, sacroiliac disarticulation. If metastasis has occurred (by the blood stream to the lungs), x-ray treatment may be tried but is usually unavailing.

Benign giant-cell tumor resembles an area of granulation tissue, filled with giant cells of the foreign body type, which has pushed the cortex of the bone aside, thinning it. There may be some fibroblastic connective

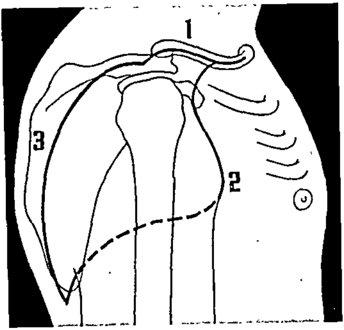

Fig. 346.—Lines of incision for interscapulothoracic disarticulation. The numbers indicate the order in which the dissections are made. (From Berman, J. K.: Surgery 18: 256, 1945.)

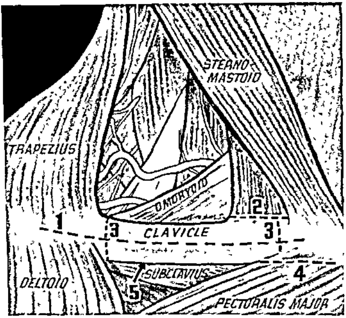

Fig. 347.—Interscapulothoracic disarticulation of the arm (continued). Diagram illustrating the antomy of the subcutaneous structures 1, Incision in the periosteum of the clavicle; 2, division of sternomastoid muscle from its clavicular origin; 3, subperiosteal removal of the lateral two-thirds of the clavicle; 4, separation of the pectoralis major muscle from the clavicles, 5, severance and lateral reflection of the subclavius and its overlying periosteum in line with medial edge of divided clavicle. (From Berman, J. K.: Surgery 18, 256, 1945.)

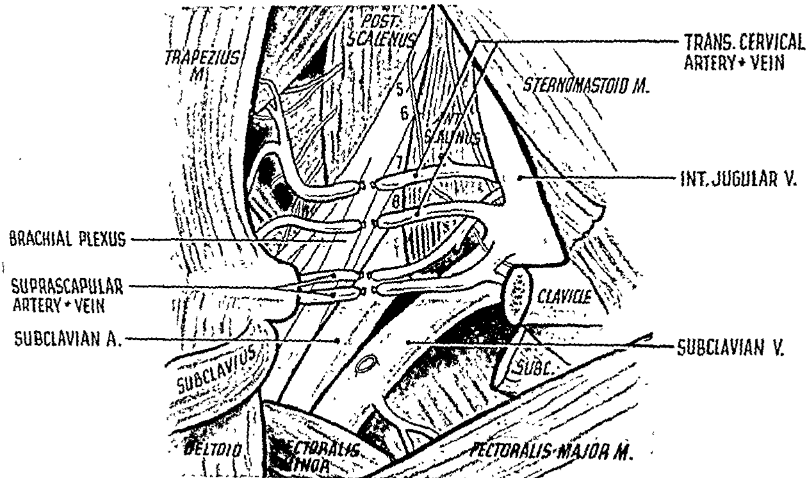

Fig. 348.—Interscapulothoracic disarticulation of the arm (continued). Diagram of the deep anatomy. The transverse cervical and transverse scapular arteries and veins have been divided between ligatures. (From Berman, J. K.: Surgery 18: 256, 1945.)

tissue and some spicules in the later stages of the tumor. Geschicter has published a chart for x-ray use showing sites of bone disease and tumors.

Although it may be difficult to distinguish different types of giant cells in histological sections, due to the manner in which they are cut or distorted, yet three main types are encountered: the foreign body type seen in infections as a rule, the Langhans' type (seen in tuberculosis and less often in syphilis), and the malignant type seen in osteogenic and other sarcomas. Some believe the so-called Langhans' type is an artifact due to a cross section of a capillary and that the peripherally placed nuclei are simply the nuclei of the endothelial cells of the capillary wall. The giant-cell tumor usually occurs near the epiphysis in young people.

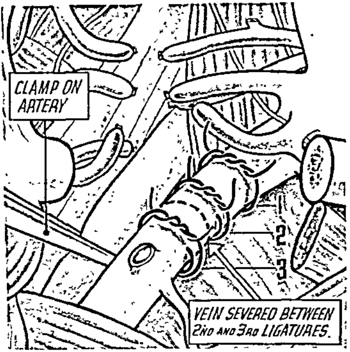

Fig. 349.—Interscapulothoracic disarticulation of the arm (continued). Method of vascular control; the subclavian artery has been clamped, the vein is tied with large silk ligatures. *1*, A simple tie; *2* and *3*, transfixed ligatures. The subclavian artery is then handled in a similar manner. (From Berman, J. K.: Surgery 18: 256, 1945.)

The tumor has been called osteoclastoma because it is thought that the giant cells are forms of osteoclasts. Two main varieties are encountered: (1) The so-called *cystic type* which has been described. It is probably a process of repair and is seen in (a) solitary bone cysts on the metaphyseal side of the epiphysis; (b) in the acute bone cyst which is found in a similar position; (c) sometimes in osteitis fibrosa cystica. The neoplasm tends to heal with x-ray treatment, after a fracture, or following curettement. (2) The *solid* or *noncystic type* is rare and is seen more often in adults in the lower epiphysis of the femur, radius, and upper epiphyseal end of the tibia. It may occur in the vertebrae, skull, and

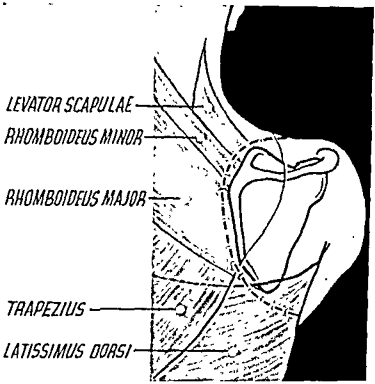

Fig. 350.—Interscapulothoracic disarticulation of the arm (continued). Line of posterior incision. The arm has been moved across the chest, displacing the scapula laterally. (From Berman, J. K.: Surgery 18: 256, 1945.)

Fig. 351.—Clinical photograph (J. B. same case as in Fig. 345) showing scar ten days after interscapulothoracic disarticulation. The wound has healed by first intention. (From Berman, J. K.: Surgery 18: 256, 1945.)

facial bones. Microscopically there are more giant cells and less fibrous tissue and very little new bone. This type tends to recur after removal. The treatment is conservative: that is, x-ray with local curettage. Should it recur, sarcoma must be suspected, although this is uncommon. The growth is related to fibrous *epulis* in the mouth.

Unicamerate cyst is a solitary bone cyst which is lined with connective tissue, contains straw-colored fluid, and has on its inner surface cholesterol crystals and foam cells. The diagnosis is made by x-ray. The treatment is curettage and filling the cavity with bone chips.

Rarer malignant tumors are adamantinoma (adamantinoblastoma) of long bones like those seen in the jaw, liposarcoma, lymphoblastoma (lymphosarcoma, Hodgkin's disease, reticulum-cell, giant follicular), hemangioendothelioma (hemangiosarcoma), and fibrosarcoma.

Ewing's tumor (angioma series—diffuse endothelioma, endothelial myeloma) probably arises from reticulum cells of the marrow or from lymphoblasts which may arise from the reticulum cells. Grossly the tumor is seen as a large growth which has thinned the cortex to an egg-shell thickness. It is light gray on cut surface and is soft, resembling brain substance. There is no bone within the tumor. The destruction is first in the marrow, then the cortex, and then soft tissue. Sometimes this break-through stimulates new bone formation in layers (onion-peel effect). The microscopic picture is a monotonous sheet of small round cells with scanty cytoplasm and round or oval nuclei that are stained evenly. The growth spreads locally, to other bones, lymph nodes, and by the blood stream to the lungs. The diagnosis is made by x-ray and biopsy. Prognosis is extremely bad. Treatment is by x-ray therapy unless a solitary lesion is found, in which case amputation may be indicated.

The Vertebral Column

The vertebral column is made up of twenty-four movable vertebrae and nine false vertebrae, which are fused to form the sacrum and the coccyx. It supports the head and ribs and, through muscular attachments, makes it possible for man to assume the upright position. Below, it rests upon the sacrum, which in turn is wedged between the pelvic bones (the ilia). The seven cervical vertebrae curve forward, the twelve thoracic backward, and the five lumbar forward again, forming an S. The sacrum is formed by five fused vertebrae which curve posteriorly, and the coccyx is made of four which curve in the same direction. Within the vertebral canal lies the spinal cord and between the individual vertebrae run the nerve roots. The vertebrae are held together by strong ligaments supported by the powerful sacrospinalis muscles. Movement of the vertebrae is made possible by the intervertebral cartilaginous discs. The cervical region possesses the widest range of movement and the dorsal region is relatively fixed except for rotation. Each intervertebral fibrocartilage is composed of a peripheral portion (annulus fibrosus) and a pulpy central portion (nucleus pulposus). The laminae are bound together by yellow elastic fibers (ligamenta flava).

Sometimes the vertebrae do not fuse posteriorly, and in extremely rare cases there is an anterior defect. This congenital defect is called *spina bifida.* If the meninges alone protrude, a *meningocele* results. This is amenable to treatment. If the cord is in the sac, a *myelocele* results and is difficult to treat. A meningocele may be

obliterated and frequently remains cured; however, a hydrocephalus may follow. *Spina bifida occulta* is a defect in which there is a failure of fusion of spinal laminae but no sac in the lower lumbar vertebrae and is often accompanied by bladder symptoms and other symptoms. The treatment consists of division of fibrous adhesions to the cord.

Many *tumors* and *cysts* occur about the sacrum and the coccyx (which is a vestigial tail). This is due to the fact that all three germ layers are represented at this site. Thus we see meningoceles, dermoids, teratomas, neurenteric cysts, pilonidal sinus (nidus of hair), adventitious bursae, glomus tumor, and osteomas. The treatment is removal of the growth if feasible.

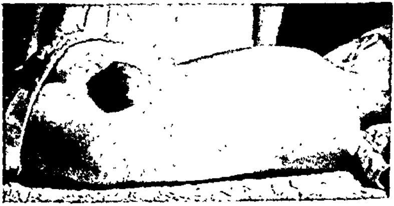

Fig. 352.—Spina bifida, with meningocele.

Fig. 353.—Sacrococcygeal tumor (teratoma) in a 2-month-old infant. Surgical removal and recovery.

The spine sometimes deviates in its curves from the normal. A large backward curve (*kyphosis*) in the thoracic region may be compensated by an exaggerated forward curve (*lordosis*) in the lumbar region. Sometimes the spine deviates and twists laterally. This is known as a rotary lateral curvature (scoliosis). These malalignments are due to postural defects in the legs or abdomen, or to structural change in the ver-

tebrae themselves, such as occur in Pott's disease (tuberculosis), or in the muscle or bony support, as in infantile paralysis, empyema, or following thoracoplasty or other chest-collapsing operations.

The side to which the convex portion extends is not always predictable due to the action of abdominal and other muscles. Following thoracoplasty in adults, the convex portion usually but not invariably points toward the operated side. This is possibly due to the fact that the musculature is disturbed and that the muscles on the opposite side, being normal, contract. Also, the support for the operated side is lost, permitting the convex portion to protrude into that direction. If the musculature is suddenly paralyzed as in poliomyelitis, the concave portion may point to the paralyzed side due to the support on the unaffected side and the lack of support on the paralyzed side. However, in children, this is entirely unpredictable due to the fact that the spine is growing; thus the convex portion may point to the paralyzed side. Also, the variables which occur as a result of groups of muscles which may remain intact renders the entire problem unpredictable. In chronic inflammatory disease of the chest, such as chronic empyema, there will be a tendency for the entire half of the chest to contract down on the affected side. The concave portion, therefore, will face the affected side.

The treatment of the functional types is support by brace or cast and special corrective exercises. Structural types may require spinal fusion operations (of the Albee or Hibbs type).

Fractures and dislocations of the vertebrae occur as a result of severe trauma. As in skull fractures, the seriousness of the injury lies not so much in the fracture or dislocation of the bone as in the damage which may have been done to the cord. This was especially true during World War II when high velocity bullets literally tore gutters in the backward curves (thoracic and sacral) of the spine as soldiers crawled on their bellies. Here the heat of the missiles burned the cord, destroyed large sections and producing paraplegias (see Chapter 18). The treatment is immobilization in a plaster shell, with head traction by tongs if necessary. The slightest movement may impinge a section of the cord and cause paralysis or even death (if the fracture is in the cervical region). Therefore, the patient must be moved with extreme caution. War injuries were treated with greater success by open operation.

Lesser injuries, such as sacroiliac or lumbosacral strain or sprain, produced so-called *chronic backache.* Outlines of the types of pain associated with the various pathological conditions and their causes are given in Tables XXV and XXVI.

Slipping forward of the fifth lumbar vertebra is known as spondylolisthesis. Prespondylolisthesis (spondylolysis, rachischisis, spondyloschisis) is a separation of the neural arch and may be associated with protrusion of the intervertebral disc. Either of these lesions may cause backache. Herniation of fascial fat, traumatic spondylitis (Kümmell's disease); vertebral epiphysitis, and other types of spondylitis may also cause pain. The treatment is by supports and x-ray and surgery where indicated (fusion in spondylolisthesis, removal of disc, or fascial fat herniation).

Spondylitis (hypertrophic, osteoarthritis, degenerating, nonankylosing) may produce pain not only in the back but in the abdomen as well. This is due to irritations of the nerve trunks. Gall bladder, kidney, appendiceal, and pelvic disease may be mimicked. However, in spondylitis rest in bed ameliorates the symptoms. Furthermore, the area of skin innervated by the affected nerves shows changes (becoming moist, cyanotic,

TABLE XXV

PARTICULAR TYPES OF PAIN ASSOCIATED WITH BACKACHE

(From Ghormley, R. K.: Backache. Examination and Differential Diagnosis, J. A. M. A. 125: 412, 1944.)

	TYPE OF PAIN PRESENT			
	STATIC, RELIEVED BY REST	MORNING, WITH OR WITHOUT "JELLING"	NOCTURNAL	CONSTANT
Probable pathological condition present	Traumatic spondylitis Spondylolisthesis Spondylolysis Old fractures of vertebrae Fractures of facets and pedicles Perivertebral traumatic changes	Usually inflammatory lesions Myositis Spondylitis deformans Fibrositis Traumatic injuries with superimposed inflammation	Associated with neurological conditions Tumors of the spinal cord Lesions of discs Obscure types, no demonstrable lesion May be forerunner of spondylitis	Malignant lesions, primary or secondary Other tumors of spinal cord Some lesions of discs Acute infection, such as osteomyelitis or infection of intervertebral disc

TABLE XXVI

LESIONS WHICH OFTEN UNDERLIE PAIN IN LOWER PART OF THE BACK

(From Ghormley, R. K.: Backache. Examination and Differential Diagnosis, J. A. M. A. 125: 412, 1944.)

	GENERAL TYPE OF LESION PRESENT					
	POSTURAL STRAIN	STATIC OR POST-TRAUMATIC	RHEUMATIC	INFECTIOUS (OTHER TYPES)	SENESCENT	NEOPLASTIC
Probable pathological condition present	Abnormal lordosis Adolescent; other types of round back Obesity Faulty body and foot mechanics	Spondylolisthesis Defective pedicles Old fractures (Kümmell's) Fractured facets Fractured pedicles Thin discs; protruded discs Hypertrophic and post-traumatic changes Congenital anomalies	Infectious arthritis Spondylitis deformans Myositis	Tuberculosis—benign osteitis—osteitis deformans Intervertebral discs, inflammatory Brucella abortus Typhoid spine	Senile osteoporosis Senescent and hypertrophic arthritis	A. Malignant myeloma Metastatic malignant lesion Primary sarcoma Ewing's tumor B. Benign osteoma and osteochondroma Giant-cell tumor Hemangioma

and cold) due to sympathetic nerve involvement. In lumbosacral sprain, pain may be referred to the inguinal region or the front of the legs, whereas in sacroiliac sprain, pain is usually referred down the sciatic nerve. The more acute type of spondylitis occurs in the young. It is also known as the rheumatoid type (atrophic, ankylosing, proliferative Marie-Strümpell arthritis, spondylitis rhizomélique). The symptoms are severe and the end result the so-called "poker spine." Treatment is by x-ray therapy and immobilization with braces or supports.

Fig. 354.—Severe degree of rotary lateral curvature of the spine. No bone disease. Condition resulted from anterior poliomyelitis.

Rarely a displaced *nucleus pulposus* (from the primitive notochord) may produce pressure on the spinal cord, causing pain or impaired motor function. This demands removal of the nucleus. Still more rarely, an hypertrophied *ligamentum flavum* may produce symptoms demanding its removal. Tuberculosis of the spinal column (Pott's disease) causes destruction of the vertebral bodies, with collapse, and the formation of a cold (iliopsoas) abscess. The treatment is that of tuberculosis elsewhere (Chapter 8), with support of the spine by casts or braces and sunlight. Occasionally, spinal fusion is required in children, often in adults.

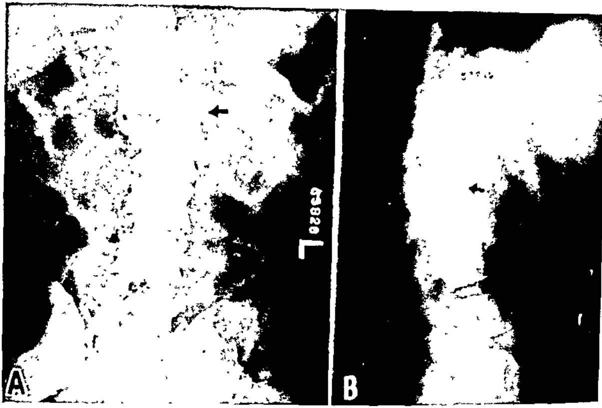

Fig 355.—*A*. Fracture of the first lumbar vertebra, with partial subluxation of the spine anteriorly and laterally. *B*. Lateral view.

Fig. 356.—Kümmell's disease of the spine (traumatic spondylitis). There are rarefaction and partial destruction of the first lumbar vertebra, which has collapsed, producing a local kyphosis.

JOINTS

Embryology, Anatomy, and Physiology

All joints *are mesodermal in origin* and differentiate. Sometimes this differentiation is a temporary stage either as a membrane limiting the extent of adjacent bones (sutura) or as cartilage *as a continuous layer in which* ossification centers occur, and the plane of articulation is marked out by unossified cartilage (synchondrosis).

In *movable joints the development is* not a temporary phase of an ossification process but is permanent. From the start these joints arise from a mass of undifferentiated mesodermic cells *lying between two groups of cells which* have differentiated into cartilage. The mass of cells is disc shaped and is in close proximity above and below with the primitive cartilage. *Around the circumference* the cells are closer together.

Fig. 357.—*Spondylolisthesis.* Note the forward dislocation of the fifth lumbar vertebra on the top of the sacrum. The entire spine is displaced slightly forward.

From this primitive mass of cells all structures of the amphiarthroidal and diarthroidal joints arise. In the latter the following structures take *origin: from the circumference,* investing ligaments and capsule lined with synovial membrane, and from its interior, fibrocartilaginous plates in the articular cavity.

The *synovial* membrane must be close to the blood supply and is, therefore, present everywhere in the joint except the free surface of the articular cartilage. *This is not* due to wear *and tear because* it is found covering the menisci of the knee. Since the epiphyses adjoining the articular cavities are produced in the joint units, the attachments of the capsule *should be limited to the* nonarticular surfaces of the epiphyses. This is true originally, but as growth progresses there are three variations: The epiphyseal line may be (a) extracapsular, (b) intracapsular, or (c) both.

The joints of the body are divided into the *synarthroses*, or immovable joints, best exemplified in the suture lines of the skull (sutura) and the occipitosphenoid articulation (synchondrosis); the *amphiarthroses*, or partially movable joints in the midline of the body, such as the symphysis pubis and the intervertebral and sternoclavicular articulations; and the *diarthroses*, or movable joints.

The diarthroidal joints are equipped for motion and weight-bearing, and the greater the movement and the weight borne, the more likely the joint is to be affected by disease. The cartilaginous caps, which are lined with the secreting synovial membrane, make motion free; and the special locking device, especially in the knee, makes weight-bearing possible. They are well supplied with blood and drain effectively into lymph channels. As in other serous cavities, circulation is not rapid, and the joints may be looked upon as the backwash of the circulation, although immunity is relatively high.

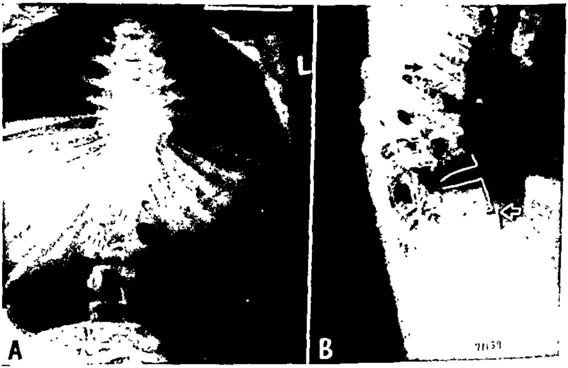

Fig 358.—*A*. Advanced tuberculosis of the spine (Pott's disease). There is collapse of the vertebrae, with calcium deposit in the soft tissues. Note the spider-web appearance of the ribs, due to vertebral collapse. *B*. Lateral view of tuberculosis of the thoracic and lumbar vertebrae. There are destruction of the bodies of the vertebrae and collapse without bone production.

The synovial membrane lines the capsular ligaments and is reflected onto the nonarticular surface of the cartilages in the joint capsule. There is a fibrosis synovial membrane which covers the areas which are subjected to pressure or strain as over the intra articular ligaments and tendons. The areolar synovial membrane lines the parts which move over underlying tissue. The adipose synovial membrane lines the fat pads which project into the joint. The membrane is in two layers: (a) internal, which is compact, cellular, and avascular; (b) external, which is vascular and, except in the fibrous type, is loosely arranged with areolar spaces and has some fat. It contains lymphatics and nerves as in the periosteum. The internal layer is analogous to the articular cartilage and the external is like the cancellous spaces of articular ends of bone.

The synovial membrane is somewhat like the peritoneum. It will absorb crystalloids readily, and colloids by the lymphatics slowly, and very large bodies are surrounded by it.

The membrane can produce osteocartilaginous bodies and is regenerated if dissected off. It may also be the seat of neoplasms (synovioma, chondroma). Due to the fact that it forms from a separate group of mesenchymal cells, it may be much larger than necessary and is thrown into folds, the synovial villi. The blood vessels form a rough circle around each extremity of the joint (circulus vasculosus). They lie opposite the reflection in the deeper connective tissue layer of the synovial membrane, and from each circle there is free inosculation over the deep surface of the membrane. The vessels are intimately connected with those of the underlying bone, especially if the *synovial reflection extends on the diaphyseal side of the epiphyseal cartilage* so as to overlie the metaphysis. In this event, bone infection may easily reach the joint and vice versa. The vessels are known as *juxtaepiphyseal* (Lexer) if they pass into the metaphysis; if not, they are called *epiphyseal*, and their connection with the metaphysis is secondary. The nutrient artery of the bone, periosteal vessels and branches from the muscular vessels, as well as the principal arteries, enter into this articular vascular anastomosis. Lymphatics are plentiful in joints. Absorption is therefore quick and is easily affected as elsewhere by pressure and motion.

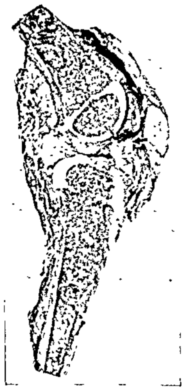

FIG. 359.—Suppurative arthritis of the knee joint. The patient was a 3-year-old boy. Arrow points to the purulent exudate in the joint cavity.

Normally synovial fluid is secreted by the synovial membrane and absorbed by the lymphatics. Trauma increases the amount of synovial fluid secreted. Absorption may be hastened by a tight bandage which increases the intra-articular pressure.

Synovial fluid lubricates joint surfaces, protects the articular cartilage from acid metabolites because it is alkaline, and helps nourish the articular cartilage. Synovial fluid is a secretion but also a transudate. It is alkaline and contains mucin, albumin, fat, inorganic salts. Its specific gravity is about 1.040; viscosity, 10.7 to 20; pH, 8.2 to 8.4; protein content, 1.6 per cent; mucin, 1.95 per cent, bilirubin, 0.5 mg.; glucose, 80 to 120 mg. per 100 c.c.; hemocytes, 50 per cubic millimeter with the following types of cells—mesothelial cells, granulocytes, and monocytes. Some erythrocytes are present.

Diseases and Injuries of Joints

Synovitis.—When the smooth glistening synovial membrane becomes injured or infected, it becomes inflamed as do other tissues, throwing out an excessive amount of synovial fluid for protection (*hydrops*, "water in the joint"). The membrane becomes thickened and rough and is therefore swollen and painful. This is known as *synovitis* and demands rest of the part.

Sprains are injuries which produce a stretching of the capsular ligaments and sometimes a tearing of these structures, resulting in a dislocation which promptly reduces itself. The symptoms are pain, swelling, and disability. For the relief of these, rest is imperative. A sprained joint should be immediately immobilized by a tight bandage, and motion should be limited for seven to ten days. X-ray examination is important because of the possibility of a fracture. A *strain* is an overstretching of muscle with tearing of some of its fibers.

Internal Derangements.—Ligamentous structures are often torn within a joint, and the cartilaginous discs may be fractured, usually as the result of severe injuries brought about from abnormal motions. Such injuries produce much pain and swelling and are exceedingly slow to heal. They are known as *internal derangements* of the joint. The semilunar cartilage has a good peripheral blood supply but a poor central one. The internal cartilage is injured almost nine times as frequently as the external. Conservative treatment leads to healing by connective tissue and should be tried. Immobilization must be maintained for weeks and even months. Often the surgeon must suture the torn ligament or excise the injured cartilage. If excised too early, chronic synovitis may result. Should small fragments of the cartilage or hypertrophied synovial villi break off in the joint, they form loose bodies (joint mice). These interfere with motion and cause the joint to lock. Diagnosis may be facilitated by air injection into the joint. They must be removed through an opening in the joint (arthrotomy).

A tendon ganglion is a cystlike tumor which communicates with the tendon sheath and occasionally with the synovial cavity of a joint. In fact, it may be associated with a low-grade inflammation of the adjacent joint. It is seen usually on the dorsum of the wrist, sometimes on the flexor surface of the wrist, and less commonly in the ankle. It is not painful, as a rule, contains a clear gelatinous substance, and is attributed to tendon injury. The treatment consists of puncture and evacuation, followed by a tight bandage. Should the ganglion recur, excision is indicated.

Classification of the Causes of Arthritis

1. Trauma
   - (a) Direct injury by blunt force
   - (b) Penetrating injuries
   - (c) Muscular action

2. Infections through the blood stream
   (a) Nonspecific infection from an acute focus
   (b) Acute rheumatic fever
   (c) Gonorrhea
   (d) Syphilis
   (e) Acute infectious diseases
       Pneumonia, typhoid, cerebrospinal meningitis
   (f) Tuberculosis
   (g) Brucellosis
3. Infections by contiguity or injury
   (a) Penetrating wounds
   (b) Osteomyelitis
   (c) Cellulitis about the joint
4. Toxins
   Allergy, serum sickness
5. Metabolic
   (a) Gout
   (b) Scurvy
   (c) Rickets
6. Neoplasms
   (a) Synovioma
   (b) Chondroma
7. Diseases of the central nervous system
   (a) Tabes
   (b) Syringomyelia
   (c) Hemiplegia
8. Hemophilia
9. Systemic
   (a) Infections (?)
       Arthritis deformans of the atrophic, ankylosing, rheumatoid, proliferative type; Still's disease; in spine: Marie-Strümpell arthritis, ankylosing spondylitis, spondylitis rhizomélique
   (b) "Wear and tear" (?)
       Arthritis deformans of the hypertrophic, nonankylosing, degenerative, osteoarthritic type
   (c) Arthritis with splenomegaly, leucopenia—Felty's syndrome

Arthritis (Nonspecific Infection Type).—The infection is usually nonspecific and is probably caused by organisms such as the streptococci and staphylococci which gain entrance through the nose or throat. In the acute septic type, a single joint is usually involved. This becomes swollen and exquisitely tender, so that the slightest motion causes excruciating pain. There is a high temperature of the septic type and great prostration. Diagnosis is easily made and confirmed by needle puncture. The fluid may be purulent (less so in streptococcic infections) and should be cultured for the organism. The treatment consists of rest in bed, transfusions if necessary, sulfonamides and penicillin, and immobilization and extension of the affected joint. Repeated aspiration or surgical drainage is often necessary. Early mobilization may minimize the resultant ankylosis.

Suppuration in a joint is governed by the same laws as suppuration elsewhere. Since lymphatic absorption is dependent on increased intra-articular pressure and motion, this can be controlled by rest and aspiration until localization occurs. Then blood capillaries and lymphatics are occluded, local immunity is established, and incision is performed for free drainage. Active motion is then useful, for pressure is relieved and adhesions will be less apt to form.

Gonorrheal arthritis also affects a single joint. It becomes painful and swollen, with less systemic reaction. Chemotherapy, antibiotics, rest, and immobilization result in recovery, as a rule, with some permanent damage. Rarely drainage is necessary.

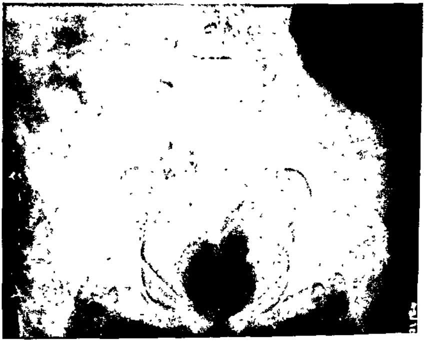

Fig. 360.—Hypertrophic arthritis of the spine (spondylitis), showing lipping of the vertebrae. The same type of arthritis also occurs in the hip joints. Note the narrowing of the joint spaces due to the atrophy of the cartilage.

Tuberculous arthritis is a local manifestation when there is tuberculosis elsewhere. The process usually affects children and is slow and insidious in its development. If left untreated, complete destruction of the joint may result, and a cold abscess will form, with multiple draining sinuses. The disease may spread to the joint by way of the metaphysis or the synovial membrane. If the latter, there may be perichondrial or superficial involvement with pannus formation, or subchondral or deep involvement with destruction of the cartilage; this is the more acute variety. Diagnosis is made by careful history, general examination for evidence of the disease elsewhere in the body, and x-ray. The treatment consists of the general treatment of tuberculosis and immobilization in a plaster cast for months until ankylosis occurs and arrest of the disease has been accomplished. Sometimes in adults it is necessary to remove the articular surfaces of the joint and produce an ankylosis (arthrodesis).

The advisability of immobilization is questioned by some. A cold abscess is thought to contain immune bodies, although these have not been isolated. All are agreed that it should be left alone unless pointing or secondarily infected. The importance of the muscular system is emphasized by Rollier and others. Prolonged immobilization leads to great muscular atrophy and diminished blood supply, with a deficiency in glycogen and immune bodies, as well as to interference with the healthy metabolism of the joints and adjacent bones. Others believe that without ankylosis there can be no arrest of tuberculosis. In general, the disease should be treated conservatively in children, more radically in adults. Streptomycin has been particularly helpful in children before widespread damage has occurred (see Chapter 8).

Syphilis of the joints occurs as a transitory synovitis in the acute secondary phase or in the congenital type. Permanent damage may occur in the tertiary stage. In tabes dorsalis a complication known as Charcot's joint occurs. There are great swelling, accumulation of fluid, overproduction of bone, and abnormal mobility. The joint is painless. The treatment is antisyphilitic therapy, penicillin in large doses, 600,000 units of procaine penicillin in oil three times a week; or, if no improvement, arsenoxide (oxophenarsine hydrochloride, dichlorphenarsine hydrochloride or phenylarsine hydrochloride), with local immobilization (see Chapter 9).

Arthritis Deformans.—A rather large and vaguely understood group of joint affections are grouped under the heading of arthritis deformans. They are divided into two main groups. The one is known as the ankylosing, rheumatoid, proliferative (that is, proliferation of marrow and subchondral and synovial connective tissue) or atrophic type; the other, as the nonankylosing, degenerative, osteoarthritic, hypertrophic, or chronic senescent type. The former occurs in young adults, occasionally in children (Still's disease). The joints are painful and swollen and the synovial membranes look like granulation tissue, and, as the name implies, they are apt to become ankylosed. Formerly, so-called silent and symptomless foci of infection were thought to be the cause. Today ankylosing arthritis deformans is looked upon more as a "system disease" affecting synovial membranes everywhere in the body. There are many examples of system diseases which occur in muscles, bone, lymph nodes, bursae, arteries, and joints. Shall we look upon these as the result of foci of infection? Is there a decreased local resistance, due to previous trauma or infection, with increased capillary permeability at the site, all of which permit an infection to "settle" in a particular type of weakened tissue? Are we confusing foci of infection with atria of infection? Do certain strains of bacteria have a selective affinity for tissues, as Rosenow has pointed out? Is a particular type of tissue susceptible because of constitutional deficiencies or diatheses? Is the disease a psychosomatic problem? These are some of the problems as yet not entirely solved. It is well to remember that the inflamed joints sel-

dom contain bacteria—except in inflammations of the acute suppurative type. The final answer is probably midway between the extremes; in other words, endogenous as well as exogenous factors must play a role. The treatment of this type is varied and includes symptomatic care, attention to vitamins, hydro- and heliotherapy, hormonal therapy (adrenal cortex, pituitary), and early motion. The nonankylosing type occurs in older individuals and leads to spur formation and calcific deposits about the joints. Heberden's nodes are nodular deformities due to small bony outgrowths about the fingers. The disease is slow and discomforting but not excruciatingly painful. Some believe it is due to "wear and tear." The treatment is dietary management, glandular therapy—thyroid and ovarian hormones and perhaps adrenocortical hormone 17-hydroxy-11-dehydrocorticosterone (compound E of Kendall), and hydro- and heliotherapy, combined with rest to the part. Surgery may be helpful. In rheumatoid arthritis the following measure may be tried, depending on the indications: careful manipulation, corrective casts, turnbuckles attached to Kirschner wires (to stretch contracted soft tissues around joints), tendon lengthening, freeing the posterior part of the articular capsule, removal of Baker's cysts (outpouching or herniation of part of articular capsule, or enlarged bursae of popliteal space), excision of rheumatic nodules, aspiration of synovial fluid, osteotomy to provide a better position of function. In osteoarthritis, operation is done usually for relief of pain. This may be accomplished by manipulation of neurectomy (as the obturator nerve in osteoarthritis of the hip) and immobilization.

BURSAE

Bursae are small synovial sacs between muscle and bone, between muscles, and over exposed surfaces. They may develop as a result of chronic irritation (adventitious). They act as hydrostatic bags, making motion free and without friction. They are filled with a small amount of fluid. A sudden tear of a muscle or tendon, or a constant strain on these structures, produces an inflammatory reaction (bursitis), with fluid. Bursae may be affected over the entire body as a result of toxins or infection. This, too, is a "system disease," vaguely understood. Due to fibrinous deposits and roughening of the smooth surfaces, motion of the part is restricted. Such lesions are seen about the shoulder (subdeltoid or subacromial bursitis), the elbow (olecranal bursitis or a "tennis elbow"), the hip (iliopectineal, gluteal, and ischial bursitis), the knee (prepatellar bursitis or "housemaid's knee"), the popliteal space (hamstring bursitis), and the ankle (Achilles bursitis). Sometimes the bursa undergoes calcification, which may be seen in the x-ray plate. The treatment in the acute stage consists of rest to the part, aspiration of fluid, diathermy, and x-ray. Sometimes surgical excision is necessary. Nature then heals the defect with fibrous tissue. Rarely bursitis may be due to tuberculosis. It results in great thickening of the bursa. Sometimes a

cold abscess forms with draining sinuses. Such bursae should be excised. Syphilitic bursitis occurs in the secondary and tertiary stages. Neoplasms of bursae may be benign (giant-cell tumor, lipoma, hemangioma, lymphangioma, fibroma and chondroma) or malignant (synovioma, fibrosarcoma, chondrosarcoma). The treatment is excision of benign growths. This may be adequate for the malignant types also, but amputation may be required.

Nature sometimes forms adventitious bursae to protect an irritated part. They develop in fibrous connective tissue which undergoes mucoid or myxomatous degeneration. They differ from true bursae in that they have no endothelial lining. Such is a *bunion*, which results from *hallux valgus*, or an outward deformity of the big toe. This usually occurs as a result of wearing shoes which are too narrow and too short. The treatment consists of protection by felt pads and proper shoes. In the late stages, excision is demanded.

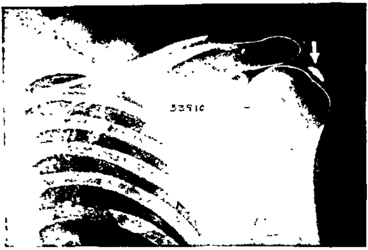

Fig. 361.—X-ray photograph, retouched, showing a calcified subacromial bursa. This disappeared under x-ray treatment.

Metatarsalgia (Morton's disease) is due to a collapse of the transverse arch of the foot. It is painful because of pressure on the plantar nerves and also because of the callus which forms over the collapsed metatarsal heads. This is not a bursa but is an attempt on the part of nature to protect these metatarsal heads. Sometimes these bones hypertrophy. Resection of the heads which are directly over the callus results in great benefit.

MUSCLES AND TENDONS

Physiology

We have noted in Chapter 19 the effects of anoxia on muscle tone. Muscle must have oxygen, not for contraction and relaxation, but for recuperation of its former state. If there is no oxygen, lactic acid accumulates and the muscle enters into rigor. Oxygen dispels lactic acid and enables the muscle to contract. Fatigue is not due to

the exhaustion of glycogen but to the high acidity. This inhibits the enzyme necessary to cause glycogen breakdown. Phosphoric acid also accumulates in muscle if oxygen is inadequate. The great role that muscle plays in the heat production of the body has already been discussed. When muscle contracts isometrically (without shortening), all the energy expended appears as heat. If it lifts a weight, 35 per cent of the energy is expended as mechanical work.

During exercise, lactic acid may appear in amounts of 3 Gm. per second. This is buffered by muscle protein, phosphates, and bicarbonates, but still there is sufficient change in blood reaction to stimulate the respiratory center so that large amounts of CO_2 are given off (Chapter 12). Lactic acid is removed in muscle by oxidation through the oxygen consumption during the recovery phase. The liver, heart, brain, and muscles not engaged in exercise help remove lactic acid which is carried to them by the blood stream. In the liver, heart, and muscles, lactic acid is removed through its conversion to glycogen. Traumatized muscle over wide areas may be a causative factor in "crush syndrome" (Chapter 14). Devitalization of muscles makes this tissue vulnerable to anaerobic infections (Chapter 6).

To test the excitability of tissue, a standard is used known as *chronaxia*. The intensity or voltage of current, which when allowed to flow for an indefinitely long period is just capable of exciting the tissue, is called the *rheobase*. *The chronaxia is the shortest duration of a current necessary for excitation when its strength is twice the rheobase.*

We have already noted in the beginning of this chapter that the muscles have important functions other than aiding in locomotion. However, they are necessary to movement and are attached to bones through their tendinous ends. Muscles undergo *atrophy* from disuse or interference with the nerve supply, or *contracture* from a constant contraction (unopposed by opposite groups of muscles) over long periods. *These are avoided by early mobilization of the arms and legs in bone or joint disease and by fixation in a neutral position.*

Flexion Contractures of the Hand

Flexion contractures of the hand produce a deformity known as "claw hand." This may result from ulnar nerve paralysis (Chapter 18), palmar skin, subcutaneous tissue, palmar fascia, or flexor tendon fibrosis; or all of these structures combined in fibrosis (Dupuytren's contracture), interference with blood supply chiefly to the flexor muscles as a result of interference with arterial supply due to injury of the branchial artery or with venous return (Volkmann's ischemic contracture).

Dupuytren's Contracture.—The cause of the palmar fascia contracture is not definitely known. Such factors as chronic trauma due to manual labor, heredity, the association with spinal cord injuries and disease (tabes dorsalis, syringomyelia, multiple sclerosis) have been mentioned as possible causes. The chief pathological change is in the palmar fascia with inflammation, proliferation of capillaries and fibroblasts, and perivascular lymphocytic infiltration. There is active proliferation of fibroblasts without other signs of inflammation and then deposition of collagen with subsequent cicatrization. Indeed the process resembles keloid formation as seen in the skin. In addition, the skin, subcutaneous tissue, and tendons may be enmeshed in scar. Certain areas may be mistaken for fibrosarcoma, but the cytology is normal. Treatment con-

sists of excision of the palmar fascia and subcutaneous scar, although the operation is difficult and recurrence is likely.

Contractures Due to Interference With Blood Supply.—These may result from arterial injury or venous occlusion. Arterial injury may result in prolonged spasm of the brachial artery with resultant ischemia and muscle degeneration with fibrosis. The pulse is absent and the extremity is cold and pale. The patient complains of severe pain. Such conditions result from fractures especially about the elbow and rarely about the knee. The treatment consists of restoring arterial supply if possible. This may be done as follows: Paravertebral injection of procaine in spasm; release of compression on the artery by blood clot, fractured bone, tight cast; and restoration of continuity of a divided artery by primary suture or venous graft.

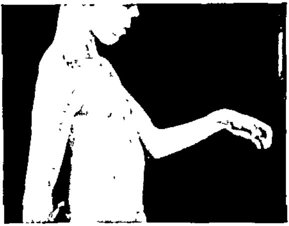

Fig. 362.—Volkmann's contracture. Note the "claw hand," with atrophy of the forearm muscles. This followed fracture of the lower end of the humerus and prolonged immobilization in a plaster cast.

Volkmann's Contracture.—A special form of contracture known as Volkmann's ischemic contracture is seen in the hand and forearm. This usually results from complete venous occlusion over relatively short periods and is seen especially in fractures about the elbow. Extravasation of blood, edema, and tight casts may be exciting factors. If this occlusion persists, rupture of the veins occurs due to extreme passive congestion. Stasis, with local asphyxia, may cause muscles to undergo necrosis, followed by fibrosis and permanent crippling. Severe pain, or discoloration of the hand in fractures about the elbow, is the first sign. Pulsation may be present in the radial artery, and early, when prevention of necrosis is still possible, there is pulsation which may be normal or weak. Regardless of the pulsation, when the pressure in the venule capillary juncture is equal to that of the arteriolar capillary pressure, circulation is impaired and ischemia results. Prior to this, however, the venules rupture and blood extravasates, thus allowing the persistent pulsation in the radial artery. The hand becomes cyanotic, cold, and

the exhaustion of glycogen but to the high acidity. This inhibits the enzyme necessary to cause glycogen breakdown. Phosphoric acid also accumulates in muscle if oxygen is inadequate. The great role that muscle plays in the heat production of the body has already been discussed. When muscle contracts isometrically (without shortening), all the energy expended appears as heat. If it lifts a weight, 35 per cent of the energy is expended as mechanical work.

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with silk (as described in Chapter 3). (6) The fibrous sheath should be reconstructed. (7) The incision in the finger is carefully closed and then after the proximal end of the graft has been sutured, the palmar or wrist incision is closed. (8) The hand is put up in flexion at the wrist (120 degrees) and at the metacarpophalangeal joints (120 degrees) (Koch).

Neuromuscular Disorders

Neuromuscular disorders (myopathies, myelopathies) are diseases and syndromes with muscular weakness and atrophy. The so-called primary muscular atrophies include the *sporadic* and *familial* diseases. The more common sporadic types are progressive muscular atrophy, including bulbar paralyses and amyotrophic lateral sclerosis, and amyotoma congenita (lack of development of muscle fibers and changes in the cortico-

Fig. 363.—Progressive muscular dystrophy. Clinical photograph of a white man (C. P.) aged 27 years who complained of generalized muscular weakness, and atrophy of the muscles of the upper arm and thigh In addition to the atrophy of the muscles of the upper arms and of the quadriceps femoris muscles, there was also some atrophy of the muscles of the back The scapula projected high in the supraclavicular spaces and the patient was unable to raise his arms above the head. His reflexes were absent or greatly diminished in most areas. Two brothers had a similar dystrophy of muscles. This man is said to exhibit a typical myopathic facies. The lips are fleshy, the eyelids tend to droop, and the smile is transverse. The involved muscles showed pseudohypertrophic masses. The patient also presented the typical "loose shoulders" of progressive muscular dystrophy There were no fibrillary tremors in the involved muscles. This particular type has been called the juvenile variety.

moist. Prevention is relatively easy. Cure is difficult, once the condition arises. Sometimes incision in the edematous tissue is necessary to relieve the venous obstruction. Fractures must be closely watched, and when pain is present in the hand, occlusive venous pressure is suspected. Some observers believe that Volkmann's contracture is arterial in origin. We prefer to regard this type as of venous origin and have therefore separated the two types. However, this may be a very difficult task clinically.

Injuries to Muscles and Tendons

Muscles and tendons may be ruptured by a severe strain and by direct trauma. Suture is often demanded. Sound muscle has a good blood supply, and proteolytic substances are minimal. If traumatized, large amounts of such substances as para-aminobenzoic acid are present, making the medium favorable for bacterial growth. In open wounds devitalized muscle makes an excellent culture medium for bacteria, especially of the anaerobic type, causing gas gangrene. Such wounds are treated by careful débridement, antitoxin, and open drainage (see Chapter 6).

Tendon repair requires a good union of the severed ends plus a smooth passageway for the tendon to move. If repair is done immediately after injury and if destruction is not too great, this may be accomplished with good results. If the tendon is badly damaged, normal uninjured tendon may be used to bridge the gap between the ends of the profundus, or one of the long extensor tendons from the the dorsum of the foot may be employed (the long extensor tendons of the lateral four toes may be removed without loss of function of the toes). After repair, the tendon must be held in place when it flexes and must be provided with a covering. The synovial sheath has a visceral layer covering the tendon and a parietal layer lining the fibrous sheath. This arrangement permits gliding movement. Substitutes for this are difficult to obtain, and therefore any part of the sheath should be saved and used as a covering. The fibrous layer may be replaced by a piece of tendon wrapped around the finger. A few rules of tendon repair may be helpful: (1) Incisions should be made so as to avoid scar contractures. The site of the incision is governed by the position of the original wound and the position of the hand at the time of injury. If the tendons are severed in extension, the distal ends will be close to the site of injury, the proximal ends far upward. If the fingers were in flexion, the distal ends of the tendons will retract downward. (2) The fibrous tendon sheath should be preserved, especially its synovial lining. In early injuries it should be opened close to its attachment to bring the tendon down. In late injuries the ventral surface may be saved in part and the dorsal surface in toto. (3) Tendons should be mobilized gently and, if fixed, the adhesions should be divided by sharp dissection. (4) Grafts should be used in widely separated old injuries. (5) Tendons should be sutured

Myotonia congenita (Thomsen's disease) is hereditary and persists throughout life with little muscular atrophy. Good results are reported with quinine.

Progressive Myelopathic Atrophies.—Infantile muscular atrophy, hypertrophic neuritis, peroneal muscular atrophy, and Friedreich's ataxia all are system diseases with changes in the central nervous system. In hypertrophic neuritis there are lesions also in the nerve trunks, and sometimes there is an associated congenital optic atrophy. The causes are unknown and there is no specific treatment.

Inflammations of Muscles and Tendons

Fibrositis.—The occurrence of infections in muscle is debatable. Healthy muscle (that is, muscle that has not been traumatized) is probably *not infected except in trichinosis. Phenomena such as Zenkerian* or hyaline degeneration of muscle fibers and the finding of aerobic bacteria in normal muscle should be mentioned. Perhaps the good blood supply of muscle has much to do with its immunity; it may also account for infections resulting after infarcts from thrombi or emboli. Tendons have a poor blood supply, and sloughing is common. In other infections the inflammation is in the connective tissue septa and should be called a *fibrositis*. Such entities as *acute lumbago* and *torticollis* belong to this group and are treated by rest, heat, massage, injection of procaine in "trigger" points, and vitamin E.

Acute *wry neck* (torticollis) is a very painful spasm of the sternocleidomastoid muscle; the patient carries the head to one side and turns the face to the opposite side from the affected muscle and fascia. The acute spasmodic type is most common. Some babies are born with a short muscle and fascia—a condition which requires surgical aid. The muscles and fascia must be divided and the child placed in a plaster cast. There is a chronic, acquired type, due to injury or infection of the lymph glands, as in tuberculosis. Sometimes tenotomy is done in the traumatic type, but rarely in the type secondary to neighboring infections. Muscular torticollis of early infancy may be due to intrauterine position, trauma at birth, and pre-existing changes within the muscle due to maldevelopment. It is thought that intrauterine torticollis is a factor in causing breech presentation. The muscle contains hard "tumors" which are thought to be hematomas or fibromas. Excision of these fibromas from the sternocleidomastoid muscle in early infancy will usually correct the deformity and thus prevent associated deformities of the head, face, and spine.

Calcification of muscle is seen in tuberculosis, hematomas, cysts, and arteriosclerosis. **Myositis ossificans traumatica** is a rare condition in which calcium is deposited in an injured muscle. It is painful and may require excision of the calcified area. In *progressive ossifying myositis* calcium may be deposited over the entire muscle system. Ammonium chloride has been advised. This condition is invariably fatal.

spinal tract). The familial type is subdivided into two groups: (a) myopathic diseases in which the histopathological changes are limited to muscles themselves or to endocrine glands; (b) inherited diseases of muscle secondary to changes in spinal cord cells—so-called myelopathic diseases.

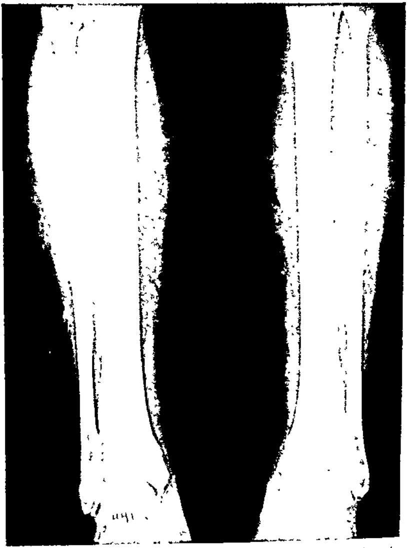

Fig. 364.—Interstitial calcinosis. There is a diffuse deposit of calcium in the muscles and around the vessels. This differs from myositis ossificans, in which there is deposition of calcium in large amounts at the site of an injury. A progressive ossifying myositis is related to this. The latter is invariably fatal.

The Progressive Myopathic Atrophies.—Myasthenia gravis is presumed to be a disorder of the myoneural junction, primarily the cholinesterase and the acetylcholine. The best treatment is neostigmine. Thymectomy may relieve some of the symptoms.

Family periodic paralysis is a hereditary disease associated with low potassium levels in the blood serum. Potassium chloride given orally is helpful.

Progressive muscular dystrophy is little understood. Vitamins are said to be helpful.

Trichinosis has been previously discussed (page 208). Echinococcus disease rarely occurs (pages 214, 741, 1091). Tuberculous myositis may be due to extension from neighboring foci (as in tuberculous spondylitis) or as a primary disease. Syphilis is seen in the secondary stage as a fibrositis and in the tertiary stage as a gumma. New growths of muscle are rare. They may be benign (fibroma, desmoid, angioma) or malignant (fibrosarcoma, rhabdomyosarcoma, angiosarcoma). Secondary carcinoma also occurs.

Tenosynovitis.—Tendons may be infected or irritated, giving rise to painful lesions. Tenosynovitis of the suppurative type may occur as a result of an injury (see Chapter 5). This requires incision and drainage. Another type (traumatic and chronic) may be due to overuse and is treated by immobilization of the part. "Trigger" finger or snapping tendon is due to either a thickening of the tendon or narrowing of the sheath. The sheath may have to be divided longitudinally to produce a cure. Acute tendinitis with calcification may be treated by aspiration and washing of tendon sheath with procaine in physiological saline and with the x-ray.

Tendon ganglions are small cystlike accumulations of jellylike fluid which is clear and white. They probably result from a low-grade inflammation developing within the joint capsule or over the periosteum of small bones about the wrist. They are treated by excision.

Rarely, *tuberculosis* attacks tendon sheaths, giving rise to an accumulation of fluid in the sheath (hydrops), with small flakes of fibrin (rice bodies). These sheaths should be excised.

New growths of tendon sheaths include lipoma, benign giant cell tumor, xanthoma, and sarcoma. Tumors should be completely excised.

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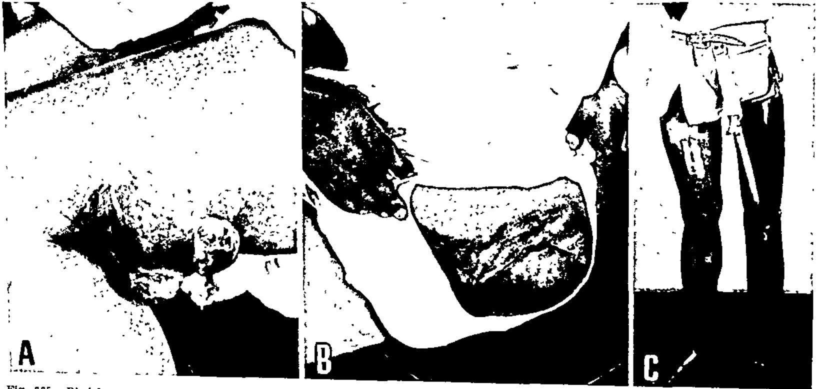

Fig. 365.—Rhabdomyosarcoma of the left thigh. The patient was a colored male aged 37 years. The growth was noted about one year before admission and had increased rapidly in size since that time. Biopsy showed the neoplasm to be a rhabdomyosarcoma. A radical amputation was done, including a disarticulation of the hip and the acetabulum. However, the interilial or hind quarter disarticulation was not deemed necessary after sampling the inguinal nodes. *A*. Clinical photograph of the neoplasm before surgery. *B*. Photograph showing the healed stump. *C*. Photograph showing the prosthesis. A special platform was built and this patient has been able to carry on his work on the artificial leg. At the end of two years the patient was still alive without metastases or recurrence.

Chapter 22

GLANDS

There are many structures, widely diff[illegible] their anatomy, physiology, and development, known as glands. [illegible] includes the following structures under the term *glands:*

1. Glands producing a visible fluid or semifluid secretion, which is discharged from the cells of the gland, either directly or by a [illegible] on a free surface, on which it is useful chemically or mechanically or by which it is [illegible].

2. The so-called *ductless glands,* which possess no [illegible] or secrete substances which are directly and gradually transmitted from the cells of the gland to the blood or lymph stream and are of use in the general metabolism of the body.

3. Cytogenic or cell producing glands, not always epithelial and usually with no distinct duct, which consist of aggregations of special cells enclosed in a more or less definite framework of connective tissue and freely supplied with blood and lymph vessels. Glands of this type are concerned in the production, from the cells in the glands, of special cells, which are liberated from the gland tissue and pass away from it. Such glands are lymph glands, bone marrow, and the reproductive glands (testes and ovaries).

Glands differ widely in structure. According to their development, they are as follows: (1) Epithelial (developed from epithelial cells with or without ducts). This group includes most of the glands of the body. The epithelium is simple, variable in structure (columnar, cuboidal), also in origin, and from time to time its morphology varies with its functions. Practically all substances which are absorbed from the outside, modified, secreted, or excreted must pass through epithelium. (2) Vascular (developed in connection with vessels, as, for example, the lymph glands, the tonsils, the thymus, and the spleen). Glands are further classified into:

1. Simple glands (duct undivided)
   a. Simple tubular—undilated at end (such as the intestinal glands)
   b. Simple alveolar—dilated at end (these do not occur in mammals)
2. Compound glands (duct divided)
   a. Compound tubular glands—branched elongated tubes with no acini (such as the cardiac glands of the stomach, Brunner's glands, the bulbourethral and vestibular glands, and the kidney)
   b. Compound acinous (grapelike) or alveolar (racemose) glands—branched duct, or ducts with saccular acini on terminal branches (which include most of the glands of the body: namely, the salivary glands, the lacrimal glands, the mammary glands, etc.)
3. Actinotubular glands—branched duct with elongated, narrow acini on terminal branches (such as the pancreas)

Glands may also be divided into *exocrine* (with epithelium lining the glandular cavities, demarcated by basement membrane from the connective tissue and blood vessels); *endocrine* (not so demarcated); and *mixed* exocrine and endocrine. *Merocrine* glands (from *mero,* a part of) secrete but do not lose cells or parts of their cells in so doing. Salivary glands and pancreatic glands are examples of this group. *Eccrine* (to expel) glands are merocrine glands with ducts.

Holocrine glands (from *holo,* entirely) secrete but lose their cells by death and sloughing in the process. The sebaceous glands belong to this type.

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grown to a large and complex state and have multiple functions in addition to the production of a secretion or excretion which is carried by ducts to the alimentary canal, or to a reservoir (such as the gall bladder or urinary bladder). This group has been designated as duct glands (exocrine) to distinguish them from the ductless gland or glands of internal secretion (endocrine), which pour their products directly into the blood stream. Some glands have both exocrine and endocrine functions. The relationship of exocrine glands to immunity (the reticulo-endothelial system) and their detoxifying function are important. Moreover, they are important in blood formation, destruction, clotting, and blood volume. Their relation to general body metabolism makes of these independent organs a large system of simple epithelial and endothelial structures which usually act as independent units. None of the secretory work is done by the capillary endothelium. "We have the gland cells for that, large robust cells with a complicated protoplasmic structure"—Krogh. The capillary endothelium is permeable to the substances required by glands. However, they may act in a concerted fashion to preserve and sustain life. The endocrine and exocrine systems are certainly capable of disengaging its units into individual parts, so far as function is concerned, but each unit is influenced by, and in turn influences, other units. Examples of this are the thyroid and pituitary, liver and kidney, pancreas and liver (these are a single unit in certain fish), the parotid, sublingual, submaxillary, and lachrymal glands which are affected in Mikulicz's disease and the lymph nodes too in the syndrome, the parotid, testes or ovaries, mammary glands, and pancreas which may be involved in mumps, and the spleen, liver, and bone marrow in Banti's syndrome. Moreover, this is definitely a system which in turn is related to the autonomic nervous system.

Therefore, we shall consider in this chapter the salivary glands and their ducts, the liver with the gall bladder and the bile ducts, the pancreas and its ducts, and the spleen; also the great endocrine system, beginning with the master pituitary, and including the pineal, the thyroid, the parathyroids, the thymus, the adrenals, the ovaries, and the testes.

EXOCRINE GLANDS

The Salivary Glands

The salivary glands include the *parotid, submaxillary,* and *sublingual* glands. Smaller glands found in the lips, cheek, palate, and tongue are similar in nature, secreting a protective mucin. There are two types of salivary cells, serous and mucous. The parotid is composed entirely of serous cells, the submaxillary contains both types of cell, and the sublingual is composed mostly of mucous cells but has some serous cells. Saliva is secreted through the stimulation of the nerves of the mouth or of some sense organ other than taste. The functions of saliva are: (1) digestive, the ptyalin of the saliva acting upon the starch molecule and splitting it into molecules of disaccharide, maltose; (2) solvent action (making possible the operation of the sense of taste); (3) preparation of food for swallowing by altering its consistency; (4) cleansing action; (5) moistening and lubricating action; (6) excretory. Many organic and inorganic substances are excreted in the saliva—drugs such as mercury, potassium iodide, lead; urea in chronic nephritis; sugar, sometimes, in diabetes; calcium in parathyroid overdosage. The viruses of hydrophobia and anterior poliomyeiltis are excreted in the saliva.

The saliva plays a role in water balance. It is secreted continuously, and the amount secreted in the course of twenty-four hours may equal 1500 c.c. In dehydration states salivary secretion, along with other secretions, is suppressed. This gives a sensation of thirst and is therefore a part of the conservative mechanism designed to maintain the water balance

The *parotid gland* lies on the masseter muscle in front of the ear and extends down to the inferior angle of the mandible. It empties its secretion into the mouth through the parotid (Stensen's) duct opposite the second upper molar. The *submax-*

Apocrine glands (from *apo*, away or separation) secrete but lose a part of the cell's cytoplasm in producing the secretion. The mammary glands and certain sweat glands belong to this group (see Chapter 5). The latter are found in the axilla, around the vulva, and in the perianal region and give off a characteristic odor. The secretion accumulates in the free end of the cell. After a time this portion of the cytoplasm is sloughed but the nucleus and the rest of the cytoplasm remain intact. Soon the cell recovers and the entire process is repeated.

In this chapter will be found examples of the various types of glands. The sebaceous, sweat, and mammary glands are considered in the chapter on skin (Chapter 16). Brunner's glands, the gastric glands, and the intestinal glands are discussed in Chapter 20, the Alimentary System. The kidneys are discussed under the Excretory System, while the vulvovaginal Bartholin's glands and the corresponding Cowper's glands in the male are discussed under the Reproductive System, Chapter 23. There remains now to be described a large group of glands with special functions that are indispensable to the body economy. Other glands can only be mentioned. For example, the mucous membrane are endowed with special glands, such as the apical in the mouth, the glands of Naboth in the cervix, the periurethral glands, etc., which lubricate and protect these linings by their smooth, slightly antiseptic viscid fluid. Some glands in the body have

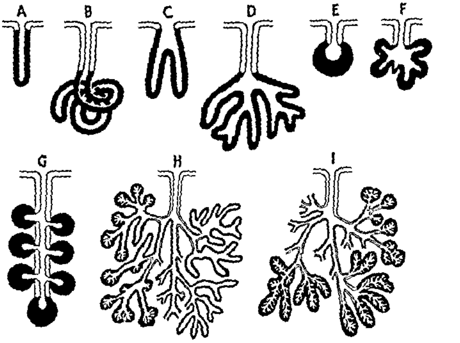

Fig. 366.—Diagram illustrating *simple* and *compound* exocrine glands (after Maximow and Bloom). The black portion is the secretory part of the gland.

A. Simple tubular gland, as found in the crypts of Lieberkuhn in the intestine.

B. Simple coiled tubular gland, as seen in the sweat glands.

C. and *D.* Simple *branched* tubular *glands*, such *as those* of the mucous membrane of the stomach and uterus (without excretory ducts), the small glands of the oral cavity, the tongue, and the esophagus, and some of the glands of *Brunner*.

E. Simple acinous or alveolar gland (*not found in mammals*).

F. and G. Simple *branched* acinous gland, as seen in the sebaceous glands of the skin and the meibomian glands of the eyelids.

H. Compound tubular gland, such as the pure mucous glands *of the oral cavity*, the cardiac glands *of the stomach*, *Brunner's glands*, the bulbourethral and vestibular glands, and the kidney.

I. Compound acinous or alveolar gland, as seen in most of the *larger exocrine* glands—albuminous and *mixed glands of the oral* cavity and respiratory passages, the pancreas, the lacrimal glands, the mammary glands, and the prostate gland.

A *secretion is* the changed *product* elaborated by the gland from *materials* brought to it; an excretion, the *separation of unchanged* waste material. It may be *difficult* to decide whether the product is the *former* or the latter or both.

the salivary flow is the normal way of cleaning the salivary ducts and the mouth. (3) Parotitis may be due to obstruction of the duct by foreign bodies such as calculi. If any of the salivary ducts are obstructed by calculi, infection may occur and will persist, leading to possible abscess formation and subsequent fistula unless the calculi are removed. (4) Parotitis from contiguous infections such as lymphadenitis, peritonsillar abscess, retropharyngeal abscess, actinomycosis, and tuberculosis of the face is secondary and will usually resolve when the primary cause is relieved. (5) Parotitis may follow injuries with or without lacerations on the outside. If the duct is torn, it must be approximated. A small cannula may be used over which the anastomosis is accomplished; then it is removed. Stenosis or atresias will result in a parotid fistula. If the duct's function cannot be restored (see Chapter V, law of fistula), the gland may be inactivated by x-ray therapy, thereby relieving an annoying fistulous discharge of saliva. (6) Parotid swelling occurs from the excretion of drugs and viruses even though a definite parotitis is not present (see discussion on functions of saliva), Chapter 20.

Tumors and Cysts of the Salivary Glands

The Parotid Gland.—*Mixed tumors* (chondrofibromyxomas) of the parotid gland might arise in at least three different ways: (1) From epithelial cells in the salivary gland which undergo mucoid degeneration into a soft jellylike substance with subsequent condensation and chemical transformation into cartilage (Ehrich); (2) from embryonal glandular rudiments (Cohnheim); (3) from remnants of the branchial arches (Virchow thought the cartilage came from Meckel's and Reichert's cartilage). The histological picture is extremely variable, so much so that pathologists have labelled mixed tumors benign and malignant. This is due to the fact that they are usually encapsulated and rarely infiltrative; they do not cause tissue destruction except for the overlying skin, and thus differ from carcinomas which involve the facial nerve; they do recur after removal, but rarely metastasize; they do not often interfere with function unless they reach a very large size. In addition, they may be composed mostly of interstitial or parenchymatous tissue, or both kinds may be present in equal amounts. Lastly, such tumors as angiomas, onchocytomas (Hürthle-cell tumors), and schwannomas may be mixed into the picture with more confusion. In the light of all available facts, it is best to regard mixed tumors as usually malignant although of low grade. Clinically they manifest themselves as painless, hard swellings. *Treatment consists of complete removal.* Formerly it was thought that it was better to wait until the tumor reached at least 3 to 4 cm. before removal so that a false capsule would form by compressing the surrounding glandular tissue. This would afford a line of cleavage, minimize injury to the facial nerve, and ensure complete enucleation. It is perhaps safer

illary gland lies under the mandible and empties its secretion through the submaxillary (Wharton's) duct on either side of the frenum, along with the ducts of the sublingual gland, which is found in this area.

Infections of Salivary Glands

Parotitis.—(1) The epidemic type known as mumps is probably due to a filtrable virus and is infectious. It may be associated with mastitis, orchitis or oophoritis, or pancreatitis (abdominal mumps). (2) Postoperative parotitis due to an ascending infection by way of Stensen's duct from the mouth and is preventable. It is usually seen in badly debilitated or severely sick patients from whom water and food by mouth are withheld. This fact and the edema occurring at the opening of the duct lead to the deduction that it is the obstruction of the duct which causes the parotitis rather than an ascending infection. The same is true in other ducts (bile duct, ureter). Formerly, when typhoid fever was

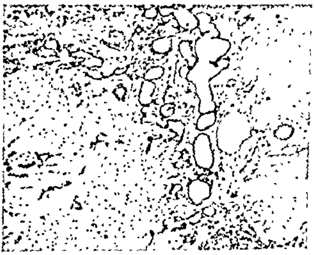

Fig. 367.—Mixed tumor of the parotid gland, showing cartilage and gland tissue.

common, the dry, dirty mouths with sores, the dehydration, and starvation which were a part of the course of the disease were often associated with this type of parotitis. Occasionally suppuration occurs, which demands incision and drainage. The patients become very ill with high temperature. The use of the duodenal suction apparatus permits the free intake of fluids after stomach and intestinal operations, although they are immediately aspirated. In addition, lemon juice and glycerine stimulate a free flow of saliva, which keeps the ducts clean. Local antiseptic solutions used as mouthwashes are useless. Attention to water and protein balance is important as a prophylactic measure. Formerly iodides were used because they are excreted in part through the salivary glands and act as an antiseptic agent. Now penicillin and streptomycin are employed. Close attention to the mouth is important in pre- and postoperative patients: cleanliness should be maintained by gentle brushing rather than by strong antiseptics, which wash out the protective mucus. Stimulation of

cylindroma type; malignant mucoepidermoid tumors, and squamous-cell carcinoma. Clinically malignant tumors are found as hard nodular painless fixed growths. Sometimes there is facial nerve paralysis early. It is impossible to be sure of the nature of a parotid tumor by palpation unless there is early facial nerve involvement. The treatment of malignant growths may be divided into three types: (1) Local excision. In early stages, when the growths are small, local excision with a wide margin is all that is necessary. Here the diagnosis is made by the pathologist as a rule. (2) Complete removal. The moderately advanced cases can be diagnosed clinically and require complete removal of the parotid gland with excision of the facial nerve if involved and a radical dissection of the neck nodes. (3) Palliative measures. In late cases with wide local involvement and distant metastases, palliative measures are indicated. These include local excision of a foul necrotic area, x-ray, and radium therapy.

The Submaxillary Gland.—This is frequently the site of secondary carcinoma from the mouth and tongue due to the close proximity of the submaxillary lymph nodes. In removing the latter, the submaxillary gland is usually taken also. Tumors which are found in the parotid also affect the submaxillary gland, requiring its removal. Retention cysts as well as cystadenomas are found, requiring removal of the gland.

The Sublingual Gland.—This is sometimes cystic and produces a swelling at the side of the frenum. This is known as a *ranula* and should be excised, for it interferes with speech and mastication.

A very rare disease, which involves all of the salivary as well as the lachrymal glands, is known as *Mikulicz's disease.* It may occur as a distinct entity with no patholgical change except round-cell infiltration, or as part of a leucemic syndrome. Treatment is x-ray.

The Liver, Gall Bladder, and Bile Ducts

The liver is developed from the entoderm of the fore gut and grows rapidly, weighing 2 grams at two months, 75 grams at birth, and 1,500 grams at maturity. The liver develops from the entoderm of the fore-gut as a median ventral growth (hepatic diverticulum). Its thick walls surround a cavity which is continuous with that of the gut. Solid cords of cells proliferate from the liver anlage and anastomose, forming the glandular portion of the liver. The duct system develops from the hollow hepatic diverticulum. This is connected with the liver by a single cord of cells which later becomes the hepatic duct. The gall bladder is at first a solid outgrowth of the caudal region of the hepatic diverticulum, which also forms the cystic and common ducts. The duct system then grows into the liver parenchyma from the hepatic diverticulum, forming the larger intrahepatic bile ducts. Gross anomalies of the external ducts are often associated with absence of internal bile capillaries. Since at first the biliary pas sages tend to be solid, a congenitally narrowed or solid state of the gall bladder and ducts is seen. Absence of the gall bladder (as seen normally in the horse and elephant) is not too rare. As a result of early splitting of ducts and gall bladder, these structures are subject to duplication. Bile is secreted in fetuses of three months; therefore babies with obstructions to the biliary tree will be jaundiced at birth. Although no main ductal connections have been demonstrated between the right and left lobes of the liver, there are undoubtedly connections between the smaller ducts of all lobes. The liver lies under the diaphragm and is held in place by its ligaments. Spaces occur be-

to remove the growth as soon as discovered, with complete removal of the tumor and surrounding gland after identification of the facial nerve so that it may be left uninjured.

Benign tumors such as adenomas and fibromas, mucoepidermoid tumors, papillary cystadenoma, and adenoma lymphomatosum should be excised. Dermoid cysts and branchial cleft cysts are sometimes found.

Malignant tumors include carcinomas, sarcomas, and miscellaneous growths such as malignant adenolymphoma (adenocarcinoma lymphomatosum; squamous carcinoma lymphomatosum), adenocarcinoma of the

Fig. 368.—Mixed tumor of the right parotid gland with malignant change and metastasis to the cervical lymph nodes. The patient, I. S., was a woman 69 years of age who had had a growth in the right parotid gland since 1918. At that time it was approximately one inch in diameter. It had enlarged steadily, but within the last two years it had grown very rapidly. At the time of admission she was unable to open her jaw and had severe pain in the right ear.

The patient was prepared for surgery and an incision was made along the inferior angle of the right mandible extending in front of the right ear. The external carotid artery was ligated just proximal to the superior thyroid artery. The right cervical and the submental nodes were removed and found to contain metastatic carcinoma from the parotid gland. The submaxillary salivary gland was also removed, but this showed no invasion. The entire right parotid gland was excised en masse and the facial nerve was preserved.

A, Clinical photograph prior to operation made from a snapshot. *B*, High-power photomicrograph of the lesion showing loose mucoid stroma with masses of fairly uniform-sized epithelial cells. Some of the strands of cells suggest a tendency to gland formation. *C*, Postoperative photograph. (Referred by Dr. D. Faris.)

as a rule. In the lungs the capillaries are compressed between epithelial plates or are without covering (see Chapter 10), allowing for a free exchange of gases. Sinusoids are not connections between arteries and veins (as capillaries are). They are subdivisions of veins. Thus, in the liver, the portal vein enters the organ and is subdivided by cords of hepatic cells into sinusoids. "The sinusoids have therefore been described as formed by the intercrescence of vascular endothelium and hepatic parenchyma." (Cunningham.) This same type of circulation is present in the Wolffian body and is probably a primitive type of vascularization, since a single vessel passing by or through an organ provides it with both afferent and efferent vessels, whereas in arteriovenous circulation there must be two vessels, the currents of which flow in opposite directions.

The portal vein carries about 75 per cent of the blood entering the liver. In this blood is insulin from the pancreas and nutrient material from the alimentary canal to be changed, detoxified, synthesized, and utilized by the liver. There are no valves in the portal vein (see Chapter 19), and normally the pressure equals about 8 to 12 mm. of Hg (108 to 162 mm. H_2O) as compared with 40 to 110 mm. H_2O in the median basilic vein. The great variations in pressure in the systemic circulation is due to the fact that the pressure as measured is the algebraic sum of the positive pressure transmitted from the arterial side and the negative pressure exerted upon the blood column by the thoracic cavity. In the portal circulation the variation is due to the enormous storage function in the operation of liver circulation. This varies as needs arise, and the outflow is controlled by a variable sluice mechanism at the hepatic venous side which is closed by histamine or opened by epinephrine or sympathetic stimulation in the experimental animal. About 1,200 to 1,900 c.c. of blood (average, 1,500 c.c.) go through the liver per minute; since the average weight of the liver is 1,500 grams, flows of 100 c.c. per 100 grams per minute occur.

Although the portal vein carries some oxygen, most of it comes from the hepatic artery which carries about 25 per cent of the blood entering the liver. The pressure in the hepatic artery is about 1200 mm. Hg. Thus, there is in the hepatic artery a small volume of circulation with a high pressure and in the portal vein a large volume of circulation with a low pressure—between the two, a freely expansible tissue framework and a common channel of exit, the hepatic vein. Both sets of vessels are under vasomotor control, and they may influence each other by direct communication or by lateral pressure. Lastly, there is an equalization of these pressures at the junction of the interlobular and intralobular venules of the liver lobules, which occurs through the communications between the veins coming from the capillaries bringing arterial blood and the portal venules. Herrick found that the rise in portal pressure was 1 mm. for every 40 mm. of arterial pressure. In the cirrhotic liver it is 1 mm. for every 6 mm. of arterial pressure. This would vary with the degree of collateral circulation, which occurs at four principal sites:

1. The veins at the site of the obliterated fetal circulation, the paraumbilical veins of the round ligament of the liver.

2. The veins at the cardiac end of the stomach which provide an outlet by way of the esophageal plexus and azygos veins to the superior vena cava.

3. Veins at the anus which connect the portal with the systemic system through the middle hemorrhoidals to the inferior vena cava.

4. Veins at sites within the abdomen where the gastrointestinal tract, or organs arising from it developed retroperitoneally. Also veins which form as a result of adhesions to the abdominal wall due to some pathological process or resulting from a previous nonspecific abdominal operation or one which is purposeful as in omentopexy (Talma) operation.

Since the liver retains such a primitive arrangement, it is easy to understand how it carries on its many functions which necessitate a free communication with the blood stream. This also explains the greater permeability of the liver capillaries to protein.

tween its superior surface and the diaphragm. The falciform ligament is a fold of peritoneum which runs from the anterior abdominal wall to the inferior margin of the liver and covers the round ligament, which is attached to the umbilicus. On the right of this is the right lobe of the liver, and on the left is the left lobe. There are also the caudate and quadrate lobes, and occasionally an extraprolongation off the right lobe, known as Riedel's lobe. The somewhat mottled appearance of the liver is due to its many lobules (about 480,000 in the dog), made of the liver cells which are arranged in cords around a central vein. In between the lobules may be seen the portal canals, which contain branches of the portal vein, the bile duct, and the hepatic artery. The liver has a double blood supply (by the hepatic artery from the celiac axis and by the portal vein from the gastrointestinal tract and the spleen, pancreas, and gall bladder). The venous blood which enters the liver has already passed through one capillary bed and in the liver passes through a second. There are two sets of capillaries within the liver itself through which its blood must go before returning to the systemic veins; the hepatic artery leads to one set of capillaries, the portal vein to another.

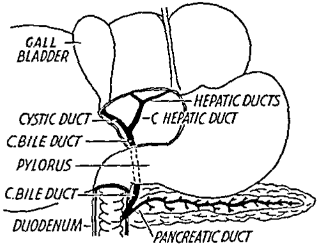

Fig. 369.—Diagram illustrating the relation of the common bile duct and the main pancreatic duct. If there is a spasm or occlusion of the ampulla of Vater, bile may flow into the main pancreatic duct, and if under sufficient pressure, may *be the cause* of acute hemorrhagic pancreatitis. Conversely, pancreatic juice may be regurgitated into the gall bladder, giving rise to acute cholecystitis. Although pancreatic juice *has been found in* the calculous gall bladder, *there is no proof* that it is the cause of gallstones.

Blood flows from the portal veins (in the portal canals) into the interlobular branches, which anastomose freely, then through the capilliform sinusoids to the central veins (intralobular veins), thence through the sublobular veins into the hepatic veins, which empty into the inferior vena cava. The arteries divide into capillaries, which empty into the capilliform sinusoids adjacent to the portal canals, thus ending in the branches of the portal vein. The arteries play a small role in hepatic circulation, supplying blood to the connective tissue about the portal canals and the surface of the liver. However, sudden occlusion of the hepatic artery is fatal in over 50 per cent of experimental animals. If penicillin is given immediately after ligation, the dogs live (Markowitz, Rappaport, and Scott). Since the liver is thought to be the source of hypertensinogen (together with the kidney), a reduction in arterial and portal vein flow reduces experimentally produced hypertension. It is not known whether this is due to a decrease in hypertensinogen or an increase in the vasodepressor substance (Davis, Tanturi, and Tarkington). The liver sinusoids (like the lacunar vessels or parasinoidal sinuses of the dura) have as thin walls as ordinary capillaries, but their diameter is greater. The close apposition of the endothelium to the cells of the liver allows a free interchange of fluids. The capillaries in general have some connective tissue about them

3. *Cardiac output and renal blood flow.* Cardiac output and renal blood flow measured by methods utilizing similar principles show that about 25 per cent of the basal cardiac output passes through the splanchnic circulation. The kidneys receive about 1,200 c.c. of blood per minute, and the brain about 800 c.c. per minute. We have noted in Chapter 18 that the cerebral circulation must be kept constant. Therefore, vascular regulation must fall upon the liver and kidneys.

4. *Variations in blood flow.* A variation of from 40 to 160 c.c. per minute per gram of liver tissue has been observed in animals. In the human being the range of blood flow is large, and all evidence points to the fact that these variations are due to general rather than to focal alterations in vasomotor activity. Moreover, this vasomotor activity affects the splanchnic arterioles also, since vasoconstriction in the liver alone would trap blood in this organ. Hepatic vasodilation would do the same thing by raising the pressure in hepatic arterial capillaries with resulting dynamic obstruction to portal outflow.

5. *Effect of exercise on blood flow.* Simultaneous measurements of blood pressure, cardiac output by the direct Fick method (Chapter 13), renal blood flow by the sodium p-aminohippurate clearance (Chapter 23), and hepatic blood flow by the method just described have revealed the following changes: (1) little change in blood pressure, (2) cardiac output almost double, (3) decreased kidney and liver blood flow (that is, the splanchnic vascular bed), with a greater decrease in the liver than the kidneys, (4) increased blood flow to the brain, heart, and muscles during exercise at the expense of the liver and kidneys, while the heart is spared the effort of supplying sufficient blood to meet the total need of exercising muscles.

6. *Effect of standing upright on blood flow.* There is a fall in cardiac output and not much change in mean arterial pressure, but there is a smaller pulse pressure due to diminished stroke volume. Vasoconstriction in the hepatoportal and renal vascular beds forms part of the diminished vascular space and the increased total peripheral resistance, accounting for reduction in local flows despite maintenance of arterial pressure. This mechanism of ischemia in the hepatic and splanchnic areas to provide blood to areas more sensitive to the effects of ischemia is part of the compensatory mechanisms described in shock (Chapter 14), hemorrhage (Chapter 13), dehydration (Chapter 11), and normal physiological variations.

If the upright position results in hepatic ischemia, then in convalescence from inflammations of the liver, especially hepatitis, patients should remain recumbent, because adequate blood flow is necessary to produce resolution (Chapter 4).

7. *Effect of pyrogenic reactions on blood flow.* With chills and fever there is an increased cardiac output, with increased blood flow through the kidney and the liver (see Chapter 4) and an increase in blood pressure. Liver function is diminished. This may be due to the heavy work of the liver in removing toxins or other pyogenic substances, thus slowing its ability to excrete bromsulfalein. These same changes occur even if fever is not present.

8 *Effect of cirrhosis on blood flow.* Atrophic cirrhosis produces a fibrotic change which results in simplification of blood vessels, changing the tortuous complex plexuses (arterial and venous) to simplified, reduced, and distorted vessels, thus reducing blood flow. Perfusion experiments of Herrick showed that the hepatic artery in a cirrhotic liver may be perfused more easily than that in the normal liver, and Dock found a decrease in arterial resistance. Studies of the estimated hepatic blood flow in cirrhosis shows it to be less than normal. Moreover, the hepatic oxygen arteriovenous difference in cirrhotic patients exceeded the normal range. Also, there is a reduction in hepatic venous oxygen saturation. In the kidney, oxygen arteriovenous difference remains about the same despite wide changes in blood flow, indicating that the variation of oxygen consumption by renal tissue is a function of blood flow. Since oxygen excretion rises when blood flow through the liver is decreased during standing, it is probably correct to assume that the increased hepatoportal oxygen excretion in cirrhosis is due to a more sluggish flow of blood through active tissues. Hepatic tissue is one of the most impor-

The liver cells are intimately connected both with the blood capillaries and radicles of bile ducts. From both sets of vessels minute channels pass into the liver cell (intracellular canals). The liver is well supplied with lymphatics, which accompany the portal and hepatic veins: the former empty into the celiac nodes; the latter pierce the diaphragm, pass through the thoracic nodes about the vena cava, and empty into the thoracic duct. A superficial set of lymphatics drains the parietal and visceral surfaces of the liver, and there are communications between the superficial and deep channels and also between the lymphatics of the gall bladder and the superficial lymphatics of the liver—hence the necessity for removing liver parenchyma in cholecystectomy for carcinoma of the gall bladder.

In addition to the polygonal cells which carry on the function of the liver, there are stellate (Kupffer) cells which are found in the sinusoids (small spaces between the liver cells). These cells have a special function which is phagocytic and are part of the *reticulo-endothelial system.* The beginnings of the biliary tract are known as bile *canaliculi* (ductus biliferi). They are small spaces between the cords of hepatic cells, which drain into interlobular ducts, that unite, forming the hepatic ducts (lying in the portal canals), which in turn come together to form the large right and left hepatic ducts. Injected specimens resemble the branches of a tree. The right and left hepatic ducts unite to form the *common hepatic duct,* which is joined by the cystic duct to form the common bile duct. This enters the duodenum at the ampulla of Vater.

The gall bladder is a blind sac which stores bile, concentrates it, and then contracts in response to a hormone (cholecystokinin) which is found in the duodenum. If the gall bladder is removed, the bile ducts dilate to take on its function in part. Although normally the bile capillaries are separated from the blood vessels by hepatic cells, if great distention of the ducts occurs due to obstruction, they may rupture, causing bile to escape into the perivascular tissue, with resulting jaundice.

Physiology of the Liver.—The liver is the largest single organ in the body with important functions. Its extirpation is fatal to animals and man, yet removal of 80 per cent of it leaves enough liver to carry on its function. Moreover, it regenerates so rapidly that within six to eight weeks it regains its normal size. We may look upon it as a large gland strategically placed between the gastrointestinal tract and the blood stream, acting as a selective barrier, metabolizing, detoxifying, and elaborating (for further physiological disposition) various substances that come to it through the portal vein.

Bradley and co-workers have introduced a long radiopaque ureteral catheter in the antecubital vein and have passed it, under fluoroscopic control, through the superior vena cava, the right atrium, the inferior vena cava, and then into one of the right hepatic veins. With this technique the following studies were made:

1. *Hepatic blood flow.* Hepatic blood flow was estimated by the bromsulfalein clearance technique. Since this drug is removed almost exclusively by the liver, the rate of intravenous infusion is equal to the rate of hepatic removal when the bromsulfalein concentration in the blood is kept constant. Dividing the calculated rate of removal by the difference between bromsulfalein concentrations in the hepatic venous and peripheral arterial (or venous) blood will yield a value which is roughly that of hepatic blood flow. There may be three sources of error in this technique: (1) some of the dye is removed by the tissues outside the liver, (2) the concentration in peripheral arterial blood may not equal concentration in the portal vein, (3) blood is sampled from only one hepatic vein and may not be representative of the liver as a whole.

2. *Normal estimated hepatic blood flow.* Normal estimated hepatic blood flow is from 950 to 1,840 c.c. per minute per 1.73 $M.^2$ of body surface. The average is about 1,500 c.c. per minute.

bile is acid (pH 5.0 to 6.0). Organic materials make up 60 per cent of its solids. Gall bladder bile is about seven times more concentrated than liver bile. Bile salts are sodium glycocholate and taurocholate. Bile pigments are derived from hemoglobin and are formed in the reticulo-endothelial cells as well as in the liver, so that the liver excretes bile pigments brought to it as such, and in addition, secretes those which it forms. Before passing through the liver cells, the bilirubin is known as "prehepatic" or reticulo-endothelial bilirubin. On passing through the liver cells, bilirubin is converted from a colloid to a crystalloid by removal of a protein molecule; it then becomes "posthepatic" bilirubin, in which form it is excreted in the feces. Here it undergoes reduction by bacteria to form urobilinogen (stercobilinogen). A part of this is excreted in the stools, and by oxidation it is converted to urobilin (stercobilin). A part of the urobilinogen is absorbed and brought to the liver for re-excretion in the bile. Normally the bilirubin and only traces of urobilin appear in the urine. Bile aids in fat digestion and absorption. It is also said to be antiputrefactive and laxative. If bile is completely excluded from the body, death ultimately results. Lately, it has been shown that bile aids in the absorption of vitamin K from the intestine, thereby facilitating the formation of prothrombin, which is necessary in blood clotting. Other functions: Bile acids promote the formation of bile and aid in the absorption of iron, calcium, and vitamins D, E, and carotene. After bile acids have performed their functions, they are reabsorbed by the intestines (80 to 90 per cent) and returned to the liver by the portal system. Some bile acid is lost by excretion in the feces and urine and still less absorbed by the lymph channels.

7. Vitamin metabolism. (a) Conversion of carotene to vitamin A. (b) Vitamin D is stored to a large extent in the liver. (c) Vitamin K is necessary for the formation of prothrombin. (d) The liver is a storehouse for vitamin B complex. Some of these factors aid in detoxification and are depleted in so-called toxic states (thyrotoxicosis, burns, toxemia of pregnancy). They aid in the oxidation of carbohydrate and the synthesis of fat from carbohydrate and protein by participation in enzyme system.

8. Blood-forming function is present in the embryo, and the liver is a storage depot for the erythrocyte maturing factor.

9. Ascites is associated with liver disease and is not due solely to the increased hydrostatic pressure in the portal system. Other factors causing it are (a) lowering of serum proteins with decrease in osmotic pressure, (b) dietary factors, (c) disturbance of ability of liver to handle water, (d) increased permeability of portal capillaries from toxins or anoxemia and causes unknown, (e) inability of liver to help destroy the antidiuretic hormone of the pituitary. It is because of the intimate relation between hepatic function and the development of ascites in some cases that the disease is listed here.

10. Iron and copper storage, blood volume regulation, and heat production.

Functional Diseases of the Liver

Hepatic Insufficiency.—Bearing these functions in mind, we may understand what is meant by *hepatic insufficiency.* Mann performed hepatectomy (removal of the liver) in dogs. They developed hypoglycemia, or low blood sugar (see 1 above), azotemia, or accumulation of nitrogen metabolites in the blood (see 2), acidosis (see 3), toxemia, high fever, and central nervous symptoms such as stupor, convulsions, and coma (see 4), bleeding from mucous membranes (see 5), and jaundice (see 6). These same symptoms in milder form are seen clinically in hepatic insufficiency.

tant sites of oxygen uptake. Augmented oxygen excretion indicates relative ischemia of hepatic tissue. Hepatic flow is reduced in cirrhosis as a result of increased vascular resistance. This acts to produce a relative ischemia of hepatic tissues in which the excretive (parenchymal) cells figure much less prominently than in the normal organ.

9. *Relation of liver blood flow to cardiovascular dynamics.* The liver plays a role in cardiovascular dynamics since it acts with the kidney as an active reservoir for daily circulatory requirements.

Among the chief functions of the liver are the following:

1. Carbohydrate metabolism. The liver stores ingested carbohydrate as glycogen. Other sources of glycogen are protein, the glyceride of fat, and lactic acid produced in the muscles. Glycogen stores are mobile.

When blood sugar is high after the ingestion of a meal, the liver stores glycogen and then reconverts it to glucose when the body requires it. Livers with adequate stores of glycogen are less susceptible to toxic agents or processes such as chloroform or anoxemia. Excess glucose is converted to fat. When there is too little glucose, fat is mobilized and partly broken down by the liver to ketone bodies. Carbohydrate inhibits this antiketogenic function.

2. Protein metabolism is one of the most important functions of the liver, and when the organ is diseased this is the last function to cease. Among the various protein functions are (a) The synthesis of amino acids into new proteins as needed for the formation of body protein; (b) the elaboration and maintenance of plasma proteins—albumin, globulin, fibrinogen, and prothrombin; the supply of proteins to the tissues is regulated through the plasma proteins; (c) storage of synthesized protein in a labile form so that it may be quickly mobilized; adeqate stores of these proteins protect the liver from the effects of various toxins, albumin, euglobulin, pseudoglobulin; (d) protein is necessary for and accelerates the formation of acholic acid; (e) deaminization; the nitrogenous portion of the amino acid molecule is converted to urea and excreted; the remainder of the molecule is metabolized as de-glucose and fat.

3. Fat metabolism. Fat circulates in the blood as neutral fat (glyceride), cholesterol esters, and phospholipids and is present in the liver in these forms. The fatty acids combined as liver phospholipids and glycerides are more unsaturated than the fatty acids found in other tissues. Liver fat comes from the ingestion of fat, mobilization from fat depots, and synthesis of fat by the liver from carbohydrate and protein.

Normally only 2 to 4 per cent of the liver weight is due to fat. As a result of toxins, excessive amounts of cholesterol and alcohol, or deficiency in choline, the liver stores fat, thereby rendering itself susceptible to the effects of hepatic toxins.

The liver is the principal site of formation of ketone bodies. Lipotrophic factors influence the amount of liver fat by preventing its deposition or increasing its rate of removal. Lecithin was first found to prevent fatty infiltration of the liver in depancreatized dogs. Later choline was shown to be the constituent of lecithin that had this effect. Other lipotropic substances are lipocaiac, inositol, and certain amino acids. Choline acts by promoting synthesis of phospholipid in the liver as well as in the intestine.

4. Detoxification of toxins through stored glycogen and carbohydrate and defense against bacteria through the Kupffer cells.

5. Blood-clotting function through the production of fibrinogen and prothrombin.

6. Production of bile (containing cholesterol, the bile salts, and the bile pigment), bilirubin and its oxidized product biliverdin, and lecithin, inorganic salts (sodium chloride and sodium bicarbonate).

Bile is secreted continuously by the liver cells in amounts varying from 500 to 700 c.c. per day. Besides acting as a vehicle for the elimination of waste products, it has many complex functions. Liver bile is alkaline (pH 8.0 to 8.6); gall bladder

2. The *degree of damage* of liver cells. This is established by the fact that the liver will hold on to some of its functions until almost completely destroyed. The most important functions of the liver and therefore those which are not impaired until there is extensive and *severe* damage are those of protein metabolism. This impairment can be detected by the estimation of serum albumin and globulin and the albumin globulin ratio, and the prothrombin level before and after administration of vitamin K. The total serum protein is not as helpful, although it may be determined quickly and very simply by the copper sulfate gravity method. Since serum globulin may be formed elsewhere than in the liver, a very high globulin and low albumin may give a normal total value. However, a *low* total serum protein is very significant when intake and protein loss are normal. Normal value of serum albumin averages 4.1 and globulin 2.7, with an A-G ratio of 1.51 (see Chapter 15). It is usually normal in hemolytic and obstructive jaundice, high and reversed in hepatocellular jaundice. The prothrombin time is taken twenty-four hours after the administration of 2 mg. menadione intramuscularly. It is prolonged in liver damage. Other tests which are difficult and which are not routinely necessary are alkaline phosphatase, total cholesterol (150 to 220 mg. per cent normal; normal in hemolytic and hepatocellular jaundice, high in obstructive jaundice), and cholesterol esters (60 per cent of total is normal).

3. *The cause of jaundice.* The various causes of jaundice will be described later in this chapter. When one examines these causes it is apparent that the jaundice may be due to: (a) obstruction, partial or complete due to causes in the bile ducts or within the liver; (b) destruction of liver cells or hepatocellular damage, local or diffuse (so-called intrahepatic jaundice); (c) hemolytic diseases; (d) various combinations of the foregoing. The surgeon is vitally interested in trying to diagnose the cause of the jaundice as early as possible so that he may remove the cause and spare the liver. Formerly exploratory operation was resorted to frequently. Now the surgeon is aware that in certain types of infectious hepatitis exploration is not only not innocuous, but dangerous. It is probably correct to assume that in all types of jaundice there is some hepatocellular damage. If this is diffuse and comes on early in the disease, the cause is probably inflammatory and not an organic obstruction. We have already indicated the tests which may be used in such cases. A positive finding is meaningless without a very careful history and physical examination together with a meticulous study of all symptoms and signs. Some of these findings will be discussed later under Jaundice. However, we should state at this time that a careful examination of the stool, the vomitus if any, and the urine can be of great help in making a diagnosis. The nurse must be taught to chart carefully, and she must be instructed as to the meaning of a gray or white or clay-colored (acholic) stool, of dark orange-colored urine, of vomitus without bile, of jaundice with normal urine (acholuric) and stools, because color is at least a clue.

Certain tests are useful in the differential diagnosis between so-called surgical and nonsurgical jaundice, and when these tests are not conclusive, then surgical exploration is the best policy to follow.

We have reviewed earlier in this chapter the physiology of bile pigment metabolism. The significant fact upon which tests are based are as follows: Bilirubin is formed in the reticulo endothelial cells from hemoglobin. As it circulates in the blood stream on its way to the liver, it is bound with a plasma protein. It does not pass into the urine. It is a colloidal compound which is readily oxidized. It is not soluble in water or Ehrlich's solution, but it is soluble in alcohol. It is known as prehepatic or reticulo-endothelial or bilirubin I or A. It is taken to the liver where it is converted into bilirubin II or B or posthepatic bilirubin. It is colloidal but behaves like a crystalloid since it is soluble in water. It is combined with bile salts, oxidizes slowly, and passes readily into the tissues when not excreted. It is soluble in water, alcohol, and Ehrlich's solution. It is supposedly freed of its protein connection. In the intestine the post-

The surgeon is vitally interested in liver function, and he attempts to evaluate this and the function of the kidney, which is intimately associated with it, by various tests. (See Chapter 2.)

Tests for Liver Function

Because of the enormous functional reserve in the liver, tests are apt to be misleading. It has been stated that if the morbid changes are patchy, then more than 80 per cent of the liver may be damaged without any variation in liver function tests. Other factors which may give rise to erroneous results are as follows: (a) Excretory tests are subject to error due to associated kidney damage, failure of the substance to be absorbed due to disease of the bowel, or too rapid excretion of the bowel. (b) Tests based upon metabolic functions of the liver are subject to the same error as in (a), and, in addition, a low or high renal threshold. (c) Urobilinogen is formed by action of bacteria in the bowel, yet this action may take place by bacteria in the bile ducts and by bacteria acting on collections of bood as in hemorrhagic cysts of the ovary. (d) There may be technical errors in executing and reading the tests. It is wise to consider the tests in the light of the history and all of the physical findings, remembering always that any laboratory test is but a symptom, and a transient one at that. Therefore, no single test, just as no single symptom, is pathognomonic of a specific liver disease. Moreover, several pathological states may be present at the same time.

Much has been written recently about "screening tests" for liver disease. While this is an excellent method of scientific investigation, the cost to a private patient for all the tests necessary to produce screening would be prohibitive. Therefore, a practical approach to the problem is the selection of such tests as are absolutely necessary to supplement the clinical findings so that a proper diagnosis may be made and prognosis given. In the following paragraphs we shall mention many of the available tests, and discuss those which we have found to be most useful.

Tests often help in three ways:

1. The *extent* of the damage. This may be revealed by a test based on a failure of one of the less important functions of the liver and which would be apparent only if the lesion were extensive. In jaundiced patients some hepatocellular damage is usually present and it will be widespread. However, the duration of symptoms must be correlated with the findings. If the illness has been brief and the test indicates a widespread injury (35 per cent retention after one hour), infectious hepatitis may be the cause, or poisons causing extensive damage. If the history indicates a longer duration, the pathology is more apt to be patchy as in obstructive types of jaundice. For this, the *bromsulfalein test* is useful. In normal persons bromsulfalein is excreted almost entirely by the liver. Five milligrams per kilogram of body weight are injected, and there should be practically no retention after thirty minutes. In hemolytic jaundice the test is normal. In hepatocellular jaundice it is elevated; also in obstructive jaundice. In this group of laboratory aids belongs the hippuric acid test. Sodium benzoate is normally detoxified by the liver by conjugating it with aminoacetic acid to hippuric acid which is excreted in the urine. Sodium benzoate, 5.9 Gm., is given by mouth, and the quantity of hippuric acid excreted in the urine is determined by hourly examination for four hours. Normally 3 to 3.5 Gm. are excreted. This test assumes normal kidney function, and therefore a phenolsulfonphthalein test should be done at the same time. *Other* tests which are used to show the extent of the liver damage are: thymol turbidity (abnormal lipoglobulin) (0 to 3 units normal; normal in hemolytic and obstructive jaundice before liver damage occurs, positive in hepatocellular jaundice), galactose tolerance, cephalin flocculation (failure of protection of gamma globulin by albumin) (0 to + normal; normal in hemolytic and obstructive jaundice, positive in hepatocellular types), and blood sugar determination (hypoglycemia).

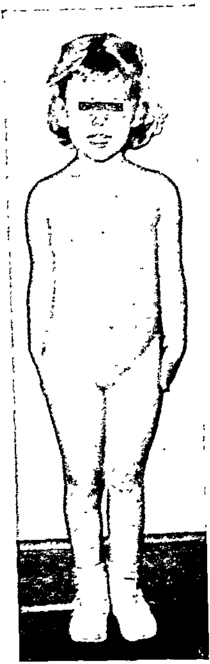

Fig. 370.—Congenital atresia of common bile duct with normal hepatic and cystic ducts and gall bladder Baby K. was brought to the hospital when 4 weeks old in July, 1945. At that time she was deeply jaundiced and the stools were white in color. The child appeared to be acutely ill. After careful study a diagnosis was made of congenital atresia of the common bile duct and operation was performed in July, 1945. At operation the liver was found to be enlarged and was firm. The gall bladder was present and contained a small amount of bile. The bile was aspirated and physiological saline was injected through a small hypodermic needle. However, it remained within the gall bladder. The common bile duct appeared to be a fibrous cord and there was some dilation of the hepatic ducts. A cholecystoduodenostomy was performed using a single layer silk suture technique. The photograph is that of the child as she appears now at 4 years of age. She is in an excellent state of health. (Referred by Dr. Herbert Call.)

hepatic bilirubin is reduced by bacterial action to urobilinogen, which is excreted in the feces in great part. Some is reabsorbed and re-excreted. Normally, traces of urobilinogen and no bilirubin are excreted in the feces.

Tests

1. Van den Bergh reaction is performed by using solution A (sulfanilic acid, concentrated hydrochloric acid, and water) and B (sodium nitrite and water). The direct reaction occurs without the addition of alcohol. Normal bile and the serum in obstructive jaundice give the prompt direct reaction; that is, the reaction of posthepatic bile. The indirect reaction requires alcohol (to separate the prehaptic bilirubin from its protein molecule). Normal serum, the serum in hemolytic jaundice, and the bilirubin formed in blood extravasations give the indirect reaction. All sera which give the direct also give the indirect reaction. A variation of the direct reaction is the delayed and biphasic reaction (color appears promptly but takes more time to change to violet); this occurs in jaundice due to extensive liver damage.

2. Icteric index is the comparison of the serum with that of a standard solution (potassium bichromate); normal, about 5 to 10. An index over 100 means complete continuous obstruction or severe and extensive destruction of liver cells. Less than 100 may indicate calculus obstruction or hepatitis of a mild type. A fluctuation reading means a stone in the common duct as a rule. The test should be repeated often to get the depth of the jaundice. With a lower icteric index (30 to 50) hemolytic or prehepatic jaundice is suspected and is proved by a test of the urine for urobilin.

3. Quantitative serum bilirubin (0.1 to 0.5 mg. per cent is normal). Icteric index of 100 usually means about 12 mg. per 100 c.c. The test is useful to know the degree of jaundice. In hemolytic jaundice it is low, 0.2 mg. to 4 mg. In hepatocellular jaundice it is high, 15.0 mg. per cent or over. In obstructive jaundice it is also high, 10 mg. per cent or over.

4. Test for duodenal damage. Using a Miller Abbott or Kantor type tube, checked for position by the fluoroscope, one can determine whether bile is entering the intestinal canal. Even a Levine tube may be used. This is especially useful in babies with possible atresia of the common bile duct, because the stool will contain some bile which is secreted in the succus entericus. In adults, small amounts indicate incomplete obstruction, blood may mean carcinoma, and no bile means complete obstruction, and, since in hemolytic jaundice stones are frequently present, producing obstruction, this method, with the addition of blood smears and fragility test, may help in the diagnosis of both conditions.

5. Examination of the urine for bilirubin and urobilinogen—normally, traces of urobilinogen and no bilirubin. In hemolytic jaundice there is no bilirubin but increased amounts of urobilinogen. In jaundice with complete obstruction, the urine contains bilirubin but usually only traces of urobilinogen (may be more due to bacteria in the obstructed ducts). Urobilinogen is found in the feces (2 to 4 Gm. per day) normally. In hemolytic jaundice, it is high; it is normal or low in hepatocellular jaundice and absent in obstructive jaundice.

In intrahepatic jaundice the urine contains bilirubin and urobilinogen in the incipient and recovery stage but very little urobilinogen in the advanced stage.

Congenital Anomalies of the Liver and Bile Ducts

These are so common that the so-called normal pattern is found in only 60 per cent of cases.

The liver varies greatly in size and position normally. Sometimes a wide tongue of liver descends from the inferior margin lateral to the gall bladder and may reach as far as the iliac crest. It is known as "Riedel's lobe." A similar process occasionally descends from the left

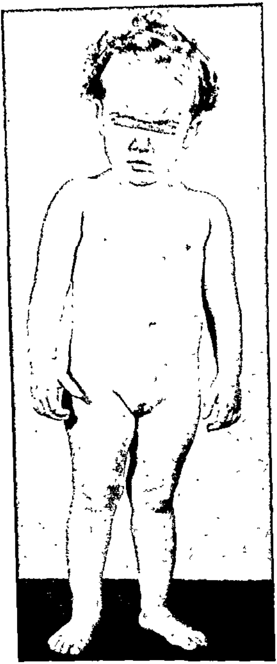

Fig 371.—Congenital absence of common bile duct, cystic duct, and absence of gall bladder. S A. S. was brought to the hospital when 2 weeks of age deeply jaundiced. She was studied for approximately two weeks, and during this time she was given many blood transfusions in an effort to correct a severe anemia. At operation no gall bladder or common duct was present. However, the hepatic ducts ended blindly at their junction. This junction was slightly dilated. An anastomosis was made between the common hepatic duct and duodenum over a piece of No. 6 catheter about 2 cm. long, using a single layer of interrupted silk stitches. The catheter passed per rectum on about the fourth day postoperative. The photograph is that of the child who is now 2 years of age and who has had no symptoms since operation. (Referred by Dr. I. Rosenbaum.)

lobe. Congenital irregularities may produce extra fossae and lobes as are commonly found in the fetus and in higher apes normally, or the liver may be divided up into a large number of distinct and separate lobes.

Arterial anomalies are extremely common. These consist of the following: (1) Accessory cystic arteries; a dozen or more different types of origin of the cystic artery have been described including abnormal position of cystic artery (anterior to common duct, to the left or right of the cystic duct, etc.). (2) Multiple hepatic arteries may be present instead of a right and left branch; there may also be an abnormal position of the right hepatic artery (to the right and anterior to common duct, under the common duct, and to the right running parallel to the cystic duct and to its right or left or posterior to it). Division of the right hepatic is fatal in over 50 per cent of the cases. (3) The gastroduodenal artery may lie anterior to the common duct and frequently a small branch from this vessel or the hepatic artery lies in the anterior wall of the common duct.

Venous anomalies and variations occur in the portal vein which bifurcates before entering the liver in 90 per cent of the cases; in 10 per cent it does not. It may receive many cystic veins and sometimes none are found. The coronary right gastric and splenic usually enter separately. Sometimes the coronary enters the splenic and also the right gastric.

The ducts are also subject to great variations. The common hepatic duct bifurcates inside the liver in 90 per cent of the cases; in 10 per cent it does not. There may be two or three cystic ducts which may all enter the common hepatic, the right hepatic, or at various levels in the common duct. The common duct may be absent, atretic, cystic, or duplicated. Duplication of the gall bladder occurs, and sometimes it is completely atretic. The cystic duct may run parallel to the common duct or enter at various angles, and the common duct may be extremely mobile so that during surgery it may assume a "/\" shape when the gall bladder is seized with forceps.

All of this discussion is extremely important because it emphasizes the care and caution that should be exercised during operations upon the biliary tract if injuries are to be avoided. It is also important because of the curative procedures that are occasionally possible in congenital atresia of the bile ducts and in cysts of the common duct.

Congenital Atresia of the Bile Ducts

We have seen how the bile ducts permeate the liver in the embryo in a solid state. It is easy to understand, therefore, that when there is atresia in the duct system, it is apt to involve all ducts in most of the cases (80 per cent in our series of twenty cases). In about 20 per cent there will be patency of the intrahepatic ducts and in one or more of the extrahepatic ducts; namely, hepatic, hepatic and part of common hepatic, and cystic. In addition, the gall bladder may be atretic or stenosed or

gall bladder formation. Whatever the cause, as the pouch increases, it consumes more and more of the bile, with less entering the duodenum.

The predominant symptoms and signs include the presence of an enlarging, painless mass in the right hypochondrium and epigastrium and increasing jaundice which is extremely slow in its development. The stools vary in color with the degree of obstruction but rarely remain white. Differential diagnosis includes congenital anomalies of the kidney and ureter and pancreas. Since they are retroperitoneal, tympany on percussion may reveal the presence of bowel anteriorly. X-ray of the gastrointestinal tract to help rule out duplication of the stomach or duodenum

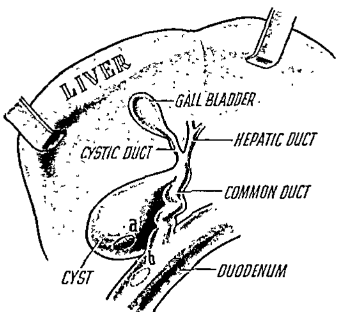

Fig. 372.—Congenital cyst of the common bile duct. The diagram is that of the condition found in a girl 4 years of age who came to the hospital complaining of pain in the abdomen of four weeks' duration, jaundice, loss of weight, and a large tumor mass in the abdomen. Her illness began about four weeks prior to admission with pain in the right upper quadrant. The patient became slightly jaundiced and this gradually deepened. On the third day of illness the referring physician stated that there was a mass about the size of an egg just to the right and below the umbilicus. On admission this tumor was easily felt and extended to three inches below the right costal border. Below the mass, filling the right lower quadrant and extending over beyond the midline, was another swelling approximately 20 cm. in diameter, and this was thought to be a cystic structure. The preoperative diagnosis was congenital cyst of the common bile duct with partial obstruction to the latter together with a greatly enlarged liver due to the obstruction The diagnosis was based upon the following facts: (1) increasing jaundice, (2) a rapidly enlarging mass in the right hypochondrium which was in a great measure cystic and which was practically painless; (3) no chills, fever, or leucocytosis; and (4) the patient was a girl and the lesion is usually encountered in the female sex.

Upon opening the abdomen a large cyst measuring approximately 30 cm. was encountered on the right side; 1400 c.c. of bile were aspirated from the cyst. The common bile duct was identified and found to be somewhat dilated and extremely tortuous and long. The gall bladder was found to be very small and was embedded in the substance of the liver, however, it did contain bile. The large cyst was attached to the common bile duct. The cyst was anastomosed to the duodenum as illustrated in the diagram at *a* and *b*. The child recovered and has remained well. The anastomosis of the cyst to the duodenum is the procedure of choice in such cases Other methods of treatment have not been very satisfactory One case reported where the cyst was extirpated was followed four years later by splenomegaly and splenic anemia for which splenectomy was necessary and this may have been due to an intrahepatic portal obstruction or thrombophlebitis of the splenic or portal vein or portal bed irritation. External drainage alone is practically always fatal and so is marsupialization.

large and filled with mucus or "white bile," being unconnected with patent ducts or distended with bile, indicating connection with a patent duct system. Rarely all the ducts are potentially open but obstructed because of retained thick mucus.

In all cases there will be varying degrees of portal cirrhosis, depending on the duration of the obstruction. The liver is hard, large, and dark green. Sometimes the spleen is also enlarged.

The chief symptom is jaundice which is usually present at birth but may be subclinical for one to two weeks. The stools are white or clay colored and of puttylike consistency. Sometimes there is a little bile pigment in the stool due to the high saturation of bile pigment in all organs. Some of this is excreted in the intestinal tract. The urine is dark in color and contains bilirubin; diagnosis is made by a process of elimination, and, therefore, surgery is not usually done before the third or fourth week of life. The following conditions must be ruled out: icterus neonatorum which usually disappears by the second week; erythroblastosis fetalis which is usually fatal early in life; the history of an Rh-negative mother with previous pregnancy and transfusion or stillbirths—presence of erythroblasts in large numbers help in excluding this; congenital syphilis; icterus from sepsis or hemolytic crises are not accompanied by acholic stools, and in the latter there is increased fragility of the red cells.

The treatment is surgical. After careful preparation with vitamin K and transfusions, a right paramedian muscle-splitting incision is made. The transversalis fascia and the peritoneum are incised transversely. This is important because where there is complete atresia of the duct system, nothing can be done, and as the liver enlarges and some ascites develops, the wound may break open unless carefully made and sutured. A systematic inspection is made starting with the gall bladder. Any duct containing bile, no matter how small, may be used. If there is bile in the gall bladder, it too may be employed. The anastomosis is made to the duodenum, and the duct is preferable to the gall bladder. We have anastomosed a patent hepatic duct to the duodenum using a piece of No. 6 catheter about 1 inch (2½ cm.) long with successful outcome. One of our patients is now 9 years old and in good health. Three notes of warning: Tie all bleeding vessels so that the operative field is clean; be sure the anastomosis is to the duodenum and not to the hepatic flexure of the colon; if all ducts seem atretic, inject saline solution—this may open the channel entirely or sufficiently to allow bile to appear in the hepatic duct which may then be anastomosed.

Congenital Cyst of the Common Duct

Choledochus cyst is rare. We have seen two cases both in female children aged 2 and 4 years. The cysts may occur in adults. The cause is unknown, but various theories have been advanced: anomalous direction of the duct, congenital stenosis, duplication, diverticulum and accessory

Infectious hepatitis is probably a virus disease, although its exact mode of transmission is unknown. It may occur sporadically or in epidemic form. The chief symptom is jaundice, although in the preicteric phase other symptoms are present; namely, chilly feeling, headache, malaise, weakness, anorexia, nausea, and occasionally vomiting. The liver is tender and enlarged with the onset of jaundice. The disease is usually over in about two weeks. However, severe cases accompanied by coma, hemorrhagic manifestations, and even death from acute hepatic necrosis may occur. There may be relapse or recurrence.

Homologous serum jaundice occurs after transfusion with plasma or whole blood. The jaundice varies in depth and persistence. There may be fever, anemia, great hepatic enlargement with or without ascites, abdominal pain, and hemorrhages. Sometimes the disease runs a rapidly *fatal course; usually it is benign. It is to be distinguished from blood* incompatibilities which are also accompanied by jaundice.

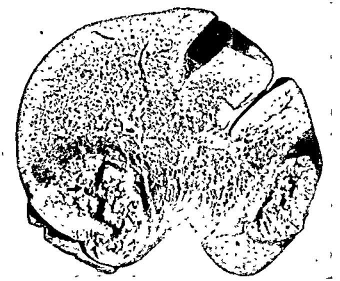

Fig. 373.—Abscessed liver in cross section. Man, aged 49 years, with amebic dysentery. Arrow points to one of the two large amebic abscesses. There was also a subphrenic abscess in this case Patient died from a perforation at the site of an amebic ulcer in the colon, with general peritonitis.

Cholangiolitic cirrhosis may be a late residue of infectious hepatitis. It is chronic with jaundice, large liver, and spleen, and it is apparently incurable.

Weil's disease is caused by a spirochete, the *Leptospira* icterohemorrhagiae. The usual vector is the gray rat. The disease manifests itself by chills and fever, great prostration, jaundice, hepatolineal enlargement, hemorrhagic tendency, and frequently renal failure. The disease can be diagnosed by finding the spirochete in the blood under dark-field illumination or by injecting blood of the patient intraperitoneally in a

or diverticula of these organs and intravenous pyelograms to rule out kidney anomalies help confirm the diagnosis.

Treatment consists of surgical exploration, examination of the cyst, and anastomosis of the cyst wall to the duodenum. Extirpation of the cyst is hazardous and may result in stricture of the duct; external drainage and marsupialization are practically always fatal. Our two cases recovered. One child is in good health eight years after operation (12 years of age now). The other is well two years after surgery.

Injuries and Diseases of the Liver

Injuries of the liver are seen following accidents and from stab and bullet wounds. The most serious is rupture of the liver, which gives rise to shock, due to intra-abdominal hemorrhage. Such injuries are usually associated with other intra-abdominal or thoracic contusion or lacerations (see Chapter 20). The diagnosis is suspected from the history, which usually reveals the site or position of the injuring force, or there may be ecchymosis or suffusion of blood over the region of the liver. There is tenderness and muscle rigidity, but it is usually generalized and is not always accurate in patients who are being revived from shock. Pain in the right shoulder (due to diaphragmatic irritation) is an accompanying symptom. Usually it is not difficult to make a diagnosis of intra-abdominal injury, but it may not be easy to name the exact site. We have observed that when the routine blood count is made in liver injury, there is a prompt leucocytosis of 16 to 20,000, with a preponderance of leucocytes. Fever soon appears, but due to shock it is not as prompt as the leucocytosis. We have not observed this in any other intra-abdominal injury, including splenic rupture. Is it due to the bacteria in the Kupffer cells and the rich blood and lymph drainage which carries the antigen into the blood stream rapidly? The treatment is prompt surgical intervention. The liver may be sutured in many ways. We have usually employed the greater omentum and used mattress sutures through it. If the omentum is ample and readily available, it may be left attached; if not, free grafts may be used. The falciform ligament may be employed in the same way, or fascia may be used. Recently Gelfoam has been used in the same manner. Dependent drainage is imperative because of the danger of bile peritonitis. If the gall bladder or external ducts have been torn, they should be repaired if possible and drainage used. If not, a catheter may be placed in the torn duct so that the bile will flow to the outside.

Infections of the Liver.—The liver stands infections well. The term hepatitis has been used rather loosely to describe an enlarged, pale, swollen liver, with rounded margins instead of the usual sharp edges. It is commonly seen in association with gall bladder or bile duct disease, and it impairs liver function (jaundice). The liver cells show cloudy swelling. This is said to improve after elimination of the gall bladder disease. This type of hepatitis may be said to be secondary.

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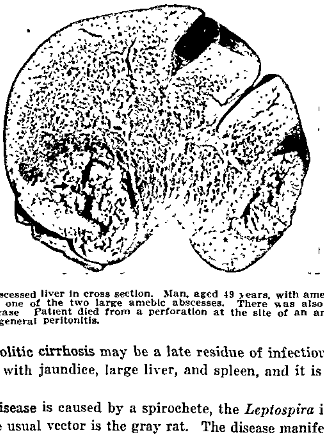

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tion). This is seen occasionally after suppurative appendicitis or diverticulitis and rarely after infections about the rectum, some of which occur postoperatively. We have seen one case after ischiorectal abscess. The liver is studded with small abscesses, giving rise to chills, fever, sweats, and mild jaundice. The treatment consists of attention to the cause of the condition; also, the use of penicillin and streptomycin. Surgical treatment is directed to the primary cause. In the liver, surgical intervention is usually unavailing unless a large solitary abscess results. This can be drained.

Subdiaphragmatic or subphrenic abscess may follow multiple or single abscess of the liver. However, it is more often seen following suppurative appendicitis, perforation of a peptic ulcer, or a gangrenous gall bladder. Pus accumulates between the diaphragm and the liver, pushing the former up and the latter down. Sometimes the infection finds its way through the lymphatics or, by perforation, into the pleural cavity, giving rise to empyema. The history, physical findings, and x-ray make the diagnosis certain. The patient shows a septicemia, with chills, fever, and a high leucocyte count. The physician's maxim is: "After appendectomy, if septic fever continues, think of abscess in the pelvis, the right lumbar gutter, or the subphrenic space." Aspiration reveals the exact location of the pus. The treatment consists of incision and drainage, usually done by removing a portion of the tenth rib on the right side, and stitching the parietal pleura in the costophrenic angle, followed by incision and drainage after forty-eight hours. This is done to prevent pleural infection.

Cirrhosis of the liver implies a hardening process which interferes with its circulation and function. In general there are two types: (1) Portal cirrhosis or the atrophic cirrhosis of Laennec. In this group belong the form associated with Banti's syndrome (intrahepatic portal hypertension), portal cirrhosis with progressive lenticular degeneration (Wilson's disease), cirrhosis of hemochromatosis, alcoholic (hobnail or gin drinkers' liver) or nutritional deficiency cirrhosis, cholangiolithic cirrhosis, chrronic hepatitis cirrhosis. (2) Biliary cirrhosis. In this group are two types: Hanot's hypertrophic biliary cirrhosis and Charcot's obstructive biliary cirrhosis. *Portal cirrhosis* is thought to represent a reaction to injury due to infections, toxic agents, avitaminosis, and many other agents and factors as yet unknown. The chief pathological change is a great increase in the fibrous tissue of Glisson's capsule on the surface and throughout its ramifications along the portal radicles. The liver becomes hard and shrunken and presents a "hobnail" appearance. The sequence of events is first a degeneration of liver cells in the periphery of the lobules, then regenerative hyperplasia of the remaining liver cells and bile ducts (compensatory hyperplasia) and repair by proliferation of the interstitial connective tissue and contraction, and, finally, as a result of this contraction, portal obstruction and the formation of col-

guinea pig and finding the spirochetes in the peritoneal fluid in ten to fourteen days. After about two weeks, serum agglutination tests may be used.

The importance of these conditions is in distinguishing them from obstructive jaundice which may be amenable to surgical intervention. A careful history may reveal that the patient came into contact with jaundiced people or recently had a transfusion. If there is bile in the stools with jaundice, the possibility of a nonsurgical jaundice will be suspected. If the patient has no bile and has had previous attacks of pain, a common duct obstruction is considered. A careful physical examination may give clues such as a nodular liver, a palpable mass indicating a nodular liver. Also, the various laboratory tests may give aid as previously discussed. Finally, surgical exploration may be necessary. While waiting for a diagnosis, a diet rich in protein and carbohydrate should be supplied, hepatotoxic substances should be diluted with intravenous medication, neutralized, and eliminated, and the patient should be kept at rest.

Specific infections include *syphilis* (Chapter 9) and *amebiasis* (Chapter 7). The latter produces a solitary large abscess caused by the Entamoeba's entrance into the portal system. The diagnosis rests upon the history, which need not include a visit to the tropics. Symptoms include diarrhea, abdominal pain, especially in the right upper quadrant, chills, fever and sweats, and great prostration. The liver is large and tender. The diagnosis is established by finding the organism in the stools. It will rarely be found in the abscess cavity but is present in the wall of the abscess. The pathological changes in the liver vary from a diffuse hepatitis to multiple small abscesses. More common is the single large one with thick violaceous pus. Treatment of diffuse hepatitis or multiple abscess consists of large doses of penicillin with emetine, alternating with Vioform. Large abscesses require aspiration in addition. This we have done in late cases with large livers without surgery. If in doubt as to the exact location, we have resected a small portion of the tenth rib, then packed with gauze for twenty-four to forty-eight hours, and then aspirated. If subdiaphragmatic abscess or empyema are present, open drainage of these collections is indicated because they are mixed infections. Syphilis may be congenital or acquired (see Chapter 9).

Tuberculosis occurs in three forms in the liver: (a) miliary; (b) conglomerate; (c) tuberculous cholangitis or pericholangitis (see Chapter 8).

Actinomycosis is not rare and may be secondary to intestinal actinomycosis by extension through retroperitoneal tissue, or directly, or by metastasis from more distant foci. The first evidence of the disease may be a subphrenic abscess (see Chapter 7).

Multiple abscess of the liver is a serious condition resulting from pylephlebitis (infection of the mesenteric veins with thrombus forma-

of the portal vein or its tributaries from infections, traumatic, or unknown causes, or combined intra- and extrahepatic causes such as portal cirrhosis plus portal vein thrombosis. The methods employed are as follows: (1) creating new venous channels by forming adventitious veins from adhesions between the liver and diaphragm or between esophageal veins and diaphragm by packing the mediastinum, or between the greater omentum and the abdominal wall—omentopexy (Talma); (2) creating portacaval shunts between the portal vein and vena cava unless a cavernomatous transformation or other complications have occurred making this procedure impossible; (3) splenectomy and end-to-side anastomosis of the splenic to the left renal vein; splenectomy alone is probably useless and may actually increase varices; (4) anastomosis of the superior mesenteric vein (proximal end) and vena cava; (5) anastomosis of other veins such as the inferior mesenteric (proximal end) and left ovarian; (6) resection of lower esophagus and upper end of stomach or entire stomach, thereby obliterating varices; (7) ligation of splenic artery to cut down flow through splenic vein and varices; (8) temporary arrest of bleeding varices by Miller-Abbott tube balloon. Of all these methods, the splenorenal shunt is perhaps most satisfactory. (See Chapter 18 and Chapter 20 under Esophageal Varices.)

The technique is as follows: First the pressure in the splenic and portal veins is ascertained. This is done to determine whether or not, in addition to intrahepatic obstruction, there may be obstruction in the splenic vein as well. If so, then splenorenal shunt is less apt to help divert blood from bleeding eophageal varices, and a mesenteric caval or portacaval anastomosis should be done. If the pressures are the same, then the splenic artery is identified, doubly ligated, and divided. The splenic vein is freed. Then the renal artery and vein are carefully dissected free. Next, the spleen is removed after a gauze-shod bulldog clamp has been placed on the splenic vein. Bulldog clamps are then applied to the renal artery and two to the renal vein. Then an end-to-side anastomosis is done using 00000 silk sutures. After the operation, pressures are again taken in the portal vein—a distinct drop is noted (10 to 12 cm. of water), because there are no valves in the portal system and blood is readily diverted from the higher pressure splenic vein into the lower pressure renal vein.

Hypertrophic biliary cirrhosis occurs in two forms: (a) Primary biliary cirrhosis or Hanot's cirrhosis and (b) secondary or obstructive or Charcot's cirrhosis.

The primary type occurs in youth and early adult life. Its cause is unknown, but many theories have been advanced: its familial tendency as in hemolytic (familial) jaundice which it resembles; its relation to infections such as typhoid; its possible relation to infectious hepatitis. The liver is large and hard, and dense fibrosis can be seen to surround the individual lobules and small bile ducts. The principal symptom is jaundice and itching, but the feces contain bile and so does the urine. There are gastrointestinal upsets. The liver is enlarged. The course of the disease is chronic, and death results in three to six years from acute degeneration of the liver cells as in acute yellow atrophy. The condition must be differentiated from portal cirrhosis (in older people),

lateral circulation. This is evidenced by (1) esophageal varices due to anastomoses between the esophageal veins with the coronary veins; (2) hemorrhoids due to anastomoses between the inferior mesenteric and hemorrhoidal veins; (3) "caput medusae" or prominent veins about the umbilicus due to anastomoses between the epigastric and portal veins by way of the paraumbilical vein of Sappey; also anastomoses form between the portal vein and vena azygos by way of the veins of the diaphragm; (4) the dilated veins of Retzius (retroperitoneal veins), connecting the inferior and superior mesenteric radicles to the inferior vena cava.

Other secondary changes are also due principally to obstruction: "vascular spiders" about the face, arms, and trunk, congestion of the mucous membrane in the gastrointestinal canal, ascites which is due to portal hypertension as well as to increased capillary permeability (from toxemia and local anoxemia) and decreased osmotic pressure (from primary and secondary hypoproteinemia), splenomegaly, interstitial fibrosis of the pancreas.

The symptoms and signs are the direct result of these changes and include those due to portal obstruction: nausea and vomiting due to congestion of the mucosa of the stomach, varices superficially and about the esophagus producing hematemesis and about the rectum producing bleeding hemorrhoids, ascites, peripheral edema, splenomegaly, and *jaundice*, which comes and goes. Two-thirds of the cases have jaundice at some time during the course of the disease and may be mistaken for external obstructive jaundice.

The diagnosis is certain when signs of portal obstruction are present. However, in its early phase the disease may resemble infectious hepatitis or obstructive jaundice if jaundice is present. Later it must be differentiated from primary or secondary carcinoma. A careful history (alcoholism, syphilitic infection, recurrent hepatitis, etc.) and physical examination coupled with laboratory aids as previously discussed will usually lead to at least a consideration of the possibility of cirrhosis. Confirmation may be had by liver biopsy taken with a needle. This method, while very informative, is not without very serious danger. Exploratory operation may be necessary. Usually careful observation soon leads to the unmistakable signs of the disease.

The treatment may be divided into medical and surgical. Both are necessary when portal obstruction is present. The medical regimen includes a diet rich in protein, high in vitamins and carbohydrates, low in fats supplemented by specific lipotropic substances (choline and cystine, methionine), whole liver extract, with vitamin B complex.

Surgical treatment is directed against the portal hypertension and its effects, whether due to intrahepatic causes, such as portal cirrhosis with or without splenomegaly, posthepatitis, cirrhosis, schistosomiasis, Chiari's syndrome (hepatic vein obstruction), or to extrahepatic causes, such as Banti's syndrome with congenital obliteration of the portal vein and cavernomatous transformation, or acquired thrombosis

thorax breast, and other situations. (b) Sarcomas—from melanoblastoma, skin melanosarcoma. Often sarcoma is associated with cirrhosis.

The diagnosis of *benign liver tumors* may be difficult. The chief symptoms are those of fullness or pressure or indigestion with or without jaundice. There is a palpable abdominal mass which is firm, movable, solitary, and rarely tender. The history of long duration will help rule out malignancy, and the absence of fever, chills, and leucocytosis makes infection improbable. The final diagnosis is made by exploration and biopsy. The treatment consists of removal of the tumor, or, if in the left lobe, a lobectomy is preferable and feasible because of the lobe's thinness, less vascularity, and more connective tissue at the insertion of the falciform ligament which renders the tissue more capable of holding sutures. More important, lobectomy permits complete removal. The various methods of resection represent different ways of dealing with hemorrhage and avoiding complications. The control of bleeding is difficult because the tumor increases vascularity and hyperemia in adjacent liver tissue, the vessels are thin walled, less contractile, and more easily torn, and the liver tissue adjacent to the tumor may be friable. Sudden hemorrhage may be controlled by pressure on the aorta above the celiac axis or by squeezing the hepatic artery in the hepatoduodenal ligament. If bulldog clamps are used on the hepatic artery, they should be removed within thirty minutes, at least temporarily. Sometimes a profound fall in blood pressure occurs after ten minutes of compression. Less severe bleeding may be arrested by gel foam, digital pressure, tourniquet of the liver proximal to bleeding edge, application of Alis clamps covered with gauze.

Methods of resection include cautery excision after suturing for hemostasis and the introduction of parallel rows of sutures, dividing between them with the scalpel. The former produces much necrosis and prevents primary closure or cover of liver edge. The latter is preferable and permits individual ligation of remaining bleeders; then the raw surface may be covered with omentum or the falciform ligament may be sutured with the free ends of the mattress hemostatic stitches.

Complications which may occur are (1) secondary hemorrhage, (2) infection in the liver edge or peritonitis; (3) metabolic disturbances such as liver shock or liver deaths, hepatorenal syndrome, hepatic insufficiency; (4) postoperative ileus and shock from bile peritonitis or from engorgement of the gastrointestinal tract if a clamp was used on the hepatoduodenal ligament, causing temporary portal obstruction; (5) persistent sinuses or bile fistulae from liver sloughs.

Primary malignant tumors are accompanied by pain over the liver area, loss of weight, anemia, weakness, and loss of appetite. There may be bleeding from esophageal varices. The tumors are multiple and hard so that the liver is a large, irregular, fixed organ. Jaundice is usually present. Secondary malignant neoplasms give rise to the same symptoms

obstructive jaundice due to stone (clay-colored stools, pain, fever, and chills), and hemolytic jaundice (increased fragility of red cells and acholuric urine). There is no specific treatment except when associated with splenic disease where splenectomy may be indicated.

The secondary type is caused by a proliferative fibrosis around the intrahepatic ducts which results from the chronic obstruction of the extrahepatic duct system. There is an associated cholangitis which also stimulates periductal fibrosis around the intrahepatic bile ducts. The causes include congenital atresia, wedged in stone in the common duct, postoperative or inflammatory stricture, and carcinoma of the ampulla, the duct, or the head of the pancreas. The symptoms and signs are those of the causative condition. The treatment consists of early removal of the obstruction or short circuiting around it. If too long a time has elapsed, the liver may be damaged beyond redemption, even after the obstruction has been relieved. The medical management as described under portal cirrhosis is followed in addition to surgical intervention.

Obstruction of the hepatic veins (Chiari's disease) is due to thrombosis of the hepatic veins where they empty into the vena cava. The obstruction may be partial or complete or complete with recavalization. As a result of the obstruction, there is central necrosis of the liver lobules, congestion of blood in this locality, fibrosis of the liver, and splenomegaly. The liver is greatly enlarged and there are ascites, pleural effusion, and leg edema. The disease may be acute or chronic, and it occurs usually between 20 and 40 years of age. The cause is unknown. The diagnosis is rarely made ante mortem or before surgery, because the clinical picture is that of portal cirrhosis. Formerly the prognosis was always fatal; now some lives have been prolonged by splenorenal shunt.

Tumors and Cysts of the Liver

Primary neoplasms of the liver are rare. They may be classified as follows:

(A) Benign: (1) hamartoma (congenital, teratoid tumors which have a relative quantitative disproportion of tissue elements normally comprising the liver but have not attained the complete pattern of the organ); hamartomas also occur in thyroid, lung, spleen, heart, mediastinum; (2) hepatoma or liver-cell adenoma; (3) cholangiomas—adenomas of the intrahepatic bile ducts, solid or cystic; (4) cholangiohepatomas of both liver-cell and duct elements; (5) neoplasms in the liver but not of specific hepatic elements—(a) cavernous hemangioma (the commonest tumor in the liver); (b) fibrous; (c) lipoma; (d) neurofibroma; (e) adrenal inclusions; (f) mesenchymoma.

(B) Malignant: (1) Liver cell carcinoma with or without cirrhosis; (2) cholangiocarcinoma; (3) sarcoma—(a) spindle-cell; (b) round-cell; (c) hemangioendothelioma.

Secondary neoplasms: (a) carcinomas secondary to carcinoma of the stomach, intestines, colon, pancreas, the organs of the pelvic cavity,

diaphragm is fixed probably due to reflex inhibition (splanchnics and vagi) caused by pain. Distention of the gall bladder will produce disturbances in blast rate rhythm and the T waves, but electrocardiogram changes in patients without clinical coronary artery disease are insignificant. There is apparently no definite electrocardiographic pattern in gall bladder disease.

The sphincter of Oddi or sphincter choledochus has a definite group of circular fibers which invest the ampulla and common duct distal and proximal to their junction. Its function seems to be that it contracts so that the gall bladder can fill. A spastic sphincter causes pain and may be the true cause of biliary colic. Intestinal distention causes a decrease in the secretion of bile and in sphincteric tone. Normally rhythmic contractions occur every two to six seconds and pressures vary between 90 to 150 mm. of water. Hydrochloric acid on the duodenal mucous membrane causes a decrease in tone; so do inhalations of amyl nitrite and Pituitrin, which at the same time increase the amplitude of contraction. Calcium chloride increases tone, as does vomiting (thus preventing a reflux of duodenal content into the duct). Morphine sulfate causes an increase in the number and amplitudes of contraction. Hypertonic solutions of glucose increase tone, whereas magnesium sulfate in the duodenum decreases tone.

Complete obstruction of the cystic duct does not produce inflammation of the gall bladder in the experimental animal if the bile is replaced by physiological saline. If bile is left within the gall bladder, inflammation results. The "white bile" usually encountered is mucus secreted by the inflamed mucosa to protect itself. Interference with the blood supply results in infarction and even gangrene. Bacterial invasion is secondary.

Complete occlusion to the common bile duct leads to dilatation of the entire ductal system with the deevlopment of fairly large interlobar communications.

Diseases of Gall Bladder and Bile Ducts

Functional disorders of the gall bladder and bile ducts occur frequently and have been listed as *dyskinesias*. Gall bladder stasis may be a forerunner of gall stones and is therefore of interest. It may be due to hypotonicity of the gall bladder or hypertonicity of the sphincter of Oddi or of the duodenum. Hypertonicity of the sphincter does occur, but its exact causes are difficult to find. Constipation of the spastic type is often associated with dyskinesia. Some observers have even advocated opening the duct and dilating or even dividing the sphincter. There is no proof that such measures are indicated unless the dyskinesia is associated with organic disease. Dyskinesia in the aged or debilitated patient may lead to hydrops of the gall bladder.

Organic diseases of biliary tract include: (1) Congenital anomalies which have been reviewed earlier in the chapter. (2) Injuries which have also been discussed and which occur usually in conjunction with injuries to the liver or other abdominal organs. In this connection we should remember that diseased gall bladders may perforate from minor injuries; normal gall bladders rarely do so. The danger in the latter instance is bile peritonitis (see Chapter 20) which may cause death by its toxic action on the capillaries and other organs, causing shock. Bacteria apparently play a minor and secondary role. Drainage is always indicated. (3) Gall stones. (4) Inflammations. (5) Obstructions. (6) Tumors and cysts. (7) Jaundice.

and signs and in addition the symptoms and signs of the primary site of the carcinoma. The treatment of primary malignancy is excisoin if possible. Even secondary carcinomas may be removed if single or if limited to one area (left lobe) and if the primary site may also be removed.

Cysts of the liver may be single or multiple, nonparasitic or parasitic, retention or due to new growth. Nonparasitic cysts are said to occur from intrahepatic obstruction of bile ducts due to congenital atresias or cicatricial obstruction. These are usually multiple but may be single or may coalesce to form one large cyst. Another type is known as cystic disease of the liver, cystic liver, cystic degeneration of the liver, polycystic liver disease, or congenital cysts of the liver. These cysts are usually more superficial and may be a part of polycystic disease in the kidneys, pancreas, or even the lungs. A third variety includes the lymphatic cysts.

Parasitic disease may also cause single or multiple cysts. Usually they are due to the echinococcus. Rarely, cystadenomas or dermoid or teratomatous cysts are encountered.

Treatment of nonparasitic cysts is by enucleation or resection; even the left lobe may be excised. A solitary cyst of the right lobe in close vicinity of the bile ducts may be marsupialized.

Echinococcus cysts of the liver may be excised if possible, or 10 per cent solution of formaldehyde may be injected and the hooklets, daughter cysts, and germinal layer removed. If this is not possible, the cyst is incised and wiped with gauze soaked in 10 per cent formaldehyde, washed with saline, and closed or drained if secondarily infected. When calcification occurs it is necessary only to remove the chitinous or germinal layer of the cyst, leaving behind the calcified wall.

The Gall Bladder and Bile Ducts

The liver cells secrete bile continuously and at a fairly constant rate. This substance, with its cholesterol, bile salts, and bile pigments, finds its way down the hepatic ducts into the common bile duct. Some of it is then poured through the ampulla of Vater into the duodenum, where it aids in the digestion of fats after a meal. Most of it, due to the contraction of the sphincter of Oddi, will course back through the cystic duct into the gall bladder for storage until fats and acids ingested call forth cholecystokinin, which causes contraction and emptying of the gall bladder. (The bile in the gall bladder is concentrated from seven to ten times by the removal of water.)

The gall bladder also acts as a pressure-regulating mechanism to take care of the continuous flow of bile, which would otherwise back into the bile ducts when the sphincter of Oddi is closed. The secretory pressure of the liver is about 30 cm. of bile pressure. The maximum expulsive power of the gall bladder is 20 to 30 cm. The sphincter of Oddi offers a resistance of 9 to 25 cm., but when in spasm the pressure may reach 75 cm. or more. After cholecystectomy, the sphincter is left more or less incompetent, with a resistance of about 15 cm.; in spite of this, however, the bile ducts dilate. The gall bladder then absorbs water, secretes mucin, and contracts to empty itself. Sudden elevation of pressure in the gall bladder or ducts will cause pain, nausea, and vomiting in dog and man. These symptoms may be abolished when the splanchnics are cut (pain) and the vagi are cut (nausea and vomiting). The right half of the

The anatomical facts collected by Sweet are as follows: (1) The presence of small pouches known as parietal sacculi (Beale) which may act as miniature gall bladders when this organ has been removed. These little sacs are lined with cuboidal epithelium. (2) The gall bladder cells are of the high columnar type, which may readily absorb sterols. (3) The gall bladder, unlike other organs, has two veins for every artery and is liberally supplied with lymphatics. (4) The mechanism by which the valves of Heister act as a baffle system, permitting stones to form within them as a mould.

Fig. 375.—*A.* Cholesterosis of the gall bladder (strawberry gall bladder). The cholesterol-containing cells are under the mucosa. *B.* High power, showing the histiocytes, which are full of lipoid material. This is seen grossly as small yellow areas which show through the mucosa.

The ideas presented by Sweet which differ from those usually accepted are: (1) Nothing leaves the gall bladder, once it has entered its lumen, except by way of the veins (crystalloids) and the lymphatics (colloids). (2) Stones form in the valves of Heister and are forced into the gall bladder by pressure within the common duct due to the contraction of the sphincter of Oddi, or they form within the lumen of the gall bladder itself, but stones in the gall bladder never leave it except by erosion through its wall into the gut, or unless removed by surgery. Stones in the common duct form because of precipitation and stasis and are usually soft (mud stones). Therefore, stones in the common duct are usually separate and distinct entities and differ from stones in the gall bladder. However, they may form in the dilated common duct when stasis is present and may resemble gall bladder stones. Therefore, the old dictum of surgeons,

Gallstones.—A stagnated pool of bile may give rise to crystallization which ultimately leads to the formation of *concretions* or *stones.* Whether this is entirely a crystallization process or the result of infection, constitutional predilection, or some chemical change is unknown. Some believe such factors as *disturbed cholesterol metabolism, bile stasis,* and *change in reaction play a role.* (Gall bladder bile is acid; liver bile is alkaline.) Should the gall bladder fail to change the reaction of the liver bile from alkaline to acid, calcium carbonate will be thrown down as a precipitate, for it stays in solution only so long as the bile is acid. Infants have been born with stones, and people ostensibly without infection may have them. Although there seems to be a hereditary tendency to obesity in patients with gallstones, this is by no means constant.

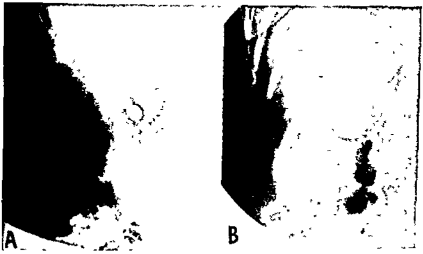

Fig. 374.—*A.* Flat plate of the abdomen, showing opaque gallstones. *B.* Gall bladder and gallstones visualized after the ingestion of tetraiodophenolphthalein.

Sweet has collected *old facts concerning the anatomy and histology of the liver* and bile ducts and has introduced new concepts of the function of these structures and the formation of gallstones.

In general, the body is equipped with balancing devices for pressures and fluids. An illustration of the former is the cerebrospinal fluid system. An illustration of the latter is the mechanism for the secretion of water and electrolytes into the upper bowel and their absorption by the lower bowel. However, glands usually secrete a substance and then have no power to alter it. The kidney is an example of the resorption mechanism if we consider the glomerulus as the beginning of the system and the tubules as the absorptive device. Sweet believes that the liver cell corresponds to the glomerulus. The bile ducts, down to and *including the gall bladder and cystic duct,* are comparable to the kidney tubule. In this system the common duct, like the ureter, is the purely excretory duct.

Another important mechanism in the body is the one *which prevents the formation of precipitates.* This may depend upon the maintenance of balance between positive and negative ions, upon the mutually protective action of colloids, and upon the lining wall of the cavities in which the fluids exist. For example, we have seen that should the limiting membrane of blood vessels (the intima) be *injured, thrombosis* occurs; should a bursa become injured, calcium may be deposited. This same mechanism may be active in the common duct, where stones form due to obstruction at the ampulla, with perhaps a *reflux of the pancreatic juice,* producing chemical irritation.

3. Hypertrophy and thickening due to edema and cholesterolosis, chronic hypertrophic cholecystitis

4. Atrophy with degeneration of mucous membrane—thin empty gall bladder—will store bile and empty feebly

5. Atrophy with fibrosis with loss of all function (storage, concentration, and expulsion of bile), chronic atrophic cholecystitis

6. Obstruction of cystic duct
   a. Intermittent with hypertrophy of gall bladder
   b. Gradually progressive with hydrops due to absorption of bile and excessive secretion of mucin
   c. Sudden and complete with
      (1) Atrophy
      (2) Acute cholecystitis
      (3) Venous obstruction causing edema and passive congestion, then interference with arterial flow when venous pressure equals arterial pressure; results in infarction and gangrene
      (4) Secondary infection as a result of (2) or (3), causing empyema of the gall bladder
      (5) Perforation with bile and bacterial peritonitis as a result of (3) or (4), or local abscess, subphrenic abscess, empyema thoracis
      (6) Infarction with erosion and formation of cholecystogastric, cholecystoduodenal, cholecystocolic or combination types of fistulae
      (7) As a result of (6) may be intestinal obstruction due to gallstone (see Chapter 20).

7. Associated diseases which may result from gallstones or which may occur in their presence
   a. Carcinoma of gall bladder may precede or follow, present in about 2 per cent
   b. Acute pancreatitis, present in about 4 per cent
   c. Pericholecystic adhesions which may cause partial obstruction or interfere with motility of duodenum or colon
   d. Interference through nervous reflex with secretory function of stomach

8. Stones may pass into the common duct in about 12 per cent and may produce:
   a. Chills, fever, and jaundice—ball valve stone; Charcot's intermittent hepatic fever (Charcot's tread)
   b. Progressive jaundice if stone is wedged
   c. Cholangitis
   d. Biliary cirrhosis of the liver (Charcot)

Symptoms and Signs of Gall Stones.—

(1) Gall stones may be present for years and remain entirely symptomless. (2) They may produce reflex symptoms of the gastrointestinal tract, both motor and secretory. (3) Gallstone colic may occur periodically. (4) The first symptoms may be those of complications such as cholecystitis, empyema, gangrene. The diagnosis is made from the symptoms and signs and the use of x-ray (cholecystogram).

Stones may remain in the gall bladder and give rise to no symptoms (silent stones). They may be single (round) or multiple (faceted) or more in the nature of small particles of sand. Usually the mucous membrane of the gall bladder is thickened, and often its columnar epithelium is studded with small cholesterol granules (strawberry gall bladder), although concretions are also found in a normal-appearing gall bladder. The stones may be made of bile pigment, cholesterol, calcium, or com-

that stones found in the common duct after a previous gall bladder operation were overlooked, is not necessarily true. (3) After removal of the gall bladder the common duct system dilates, including the parietal sacculi, and this dilatation includes the sphincter of Oddi, thereby establishing open drainage and preventing the re-formation of stones. (4) After the gall bladder dye test, the apparent emptying of this organ following a fatty meal is simply a shifting of the shadow due to absorption of the dye through the lymphatics: the dye does not leave by way of the cystic duct.

According to Sweet, the formation of stones within the gall bladder is not due to precipitation, with deposition of crystals around a nucleus. It is due to the occurrence in the bile of calcium and cholesterol in colloidal suspension. Because of the mutual protective action of colloids, certain definite patterns (such as the Maltese cross) will be laid down centripetally, within the stone, as the colloidal substance turns to a solid state. The reasons for the change in the substance after secretion may be, first, a disturbance of the absorbing function of the gall bladder, causing a damming back of the sterol; second, a reflux into the common duct of intestinal content and pancreatic juice, causing the precipitation of all the contents of bile, with the formation of biliary "mud"; third, a change in the solubility relationships of the constituents of the bile, brought about by infectious or chemical processes which injure the mucous membrane of the biliary passages and thereby permit the entry of abnormal constituents into the bile. The symptoms of biliary disease are due largely to an involvement of the motor and sensory functions of the common duct; the gall bladder takes very little part in the symptom complex. When a gall bladder is filled with dozens of faceted stones of equal size, these have formed within the valves of Heister from masses of gel like those which occur in the gall bladder and have then been pushed back into the gall bladder after they became solid.

We speak of gases of which the molecules are in a completely free state, of solutions in which the molecules are less free, of colloids in which they are still less movable, and of solids in which they move very little, retaining their positions. Sweet believes, like Liesegang, that the precipitation of a material contained in a colloidal mass by another substance which diffuses through the colloid mass does not cause a uniform precipitation but a series of rings, precipitated in rhythmic order. Such is the case in the formation of a gel of cholesterol and some calcium compound in the colloidal state.

Women are more likely to have gallstones than men. Pregnancy seems to account for this preponderance, but this is difficult to prove. No one theory as to the formation of stones is conclusive. Stasis of bile, changes in constituents of bile, infection, associated diseases and constitutional susceptibility, neurogenic disturbances, alterations in the absorptive and secretory functions due to hormonal imbalance during the active sex life have been invoked as possible causes. The association of gallstones and hemolytic jaundice has been attributed to an increased amount of bile pigment carried to the liver, causing the bile to become thick and therefore sluggish in its movement as well.

Pathology.—Gallstones are not innocuous. They may cause little change in the gall bladder but more often they lead to one or more complications. Some of these effects may be listed as follows:

1. Very little or no demonstrable change in the gall bladder, bile ducts, or liver
2. Acute inflammatory changes (acute cholecystitis usually associated with obstruction to the cystic duct but not always) which may occur without stones. Theories as to how the injury is sustained: vascular (obstruction to cystic vein and artery), chemical (pancreatic juice by reflux through spasm of sphincter of Oddi, bile), bacterial (chiefly of the streptococcus group as a secondary invader but may be primary) which may go on to gangrene and perforation

and if there has been no history of jaundice, the duct is not opened. Instead, it is our practice to open the gall bladder routinely, remove the stones, probe the common duct through the cystic duct, and then remove the gall bladder, subserously covering over the gall bladder bed with its serosa. If there is any doubt, particularly where there has been a history of jaundice, the gall bladder is opened and probed with filiform bougies and small rubber catheters. The more important complications and sequelae of cholecystectomy are (1) inflammatory stricture of the common bile duct, (2) traumatic stricture of the common bile duct, (3) "hepatorenal syndrome," and (4) "postcholecystectomy syndrome," which implies a persistence of symptoms after cholecystectomy.

While it is true that sometimes an inflammatory process (cellulitis) occurs after cholecystectomy due to secondary bacterial invasion which may cause partial destruction and cicatrization of the common duct, yet most strictures follow surgical trauma to this structure. The complication is recognized by a persistence of bile drainage or jaundice. The treatment is surgical and requires either a short circuiting around the obstruction (choledochoduodenostomy) or resection and anastomosis between the duct and the duodenum.

"*Hepatorenal syndrome*" consists of a hepatic, and later kidney, insufficiency with little or no secretion of bile, slight jaundice, slight fever, oliguria, and azotemia followed by paralytic ileus. The condition is serious and may be fatal. Many theories have been advanced to explain its cause. Among them are (1) severe trauma to the liver with hepatitis, toxemia, dehydration, hemoconcentration, anuria, (2) trauma to the liver and bile peritonitis, and (3) bacterial peritonitis, (4) serum hepatitis following transfusions, (5) infectious hepatitis. The condition as seen clinically probably has many causes. Perhaps most commonly the sequence is severe liver trauma, or operation in the presence of hepatitis, progression of the hepatitis with local peritonitis at the site of the gall bladder bed, incomplete bowel obstruction and paralytic ileus, dehydration, hypoproteinemia, and then oliguria and its effects. The condition is not seen commonly. The treatment is the same as for hepatitis and in addition decompression of the gastrointestinal tract with the Miller-Abbott tube, attention to water balance and blood volume chemotherapy.

"*Postcholecystectomy syndrome*" implies a persistence of symptoms after cholecystectomy. Causes include (a) benign stricture of common duct, (b) parenchymatous pancreatitis, (c) hepatitis, (d) residual stones in the common duct or gall bladder neck if not removed, (e) biliary dyskinesia and spastic sphincter of Oddi, (f) adhesions between pylorus or duodenum and gall bladder bed, (g) duodenal diverticulum, irritable or spastic bowel. In addition to these more or less demonstrable causes, the fact that the syndrome rarely occurs after cholecystectomy for stones but is more apt to follow cholecystectomy for cholesterolosis has led to the supposition that there is less adjustment (dilation of intrahepatic ducts) in the latter case than in the former. Finally, it is an observed

binations of these substances. (Cholesterol stones are most common.) The patient usually presents a *history of discomfort in the upper right quadrant, with attacks of indigestion* (belching, intolerance to certain foods, etc.). If a small stone begins its course down the cystic duct, there result attacks of excruciating pain, known as a *gallstone colic*. This pain is said to be due to a spasm of the sphincter of Oddi and a sudden elevation of pressure in the gall bladder or bile ducts. Therefore, sodium nitrite and magnesium sulfate are more efficient than morphine for relief. The attacks are characteristic, the *pain radiating to the back and right shoulder*. *If the stone finds its way into the common duct*, the attacks of pain are followed by jaundice and clay-colored stools (due to an absence of bile), and since a cholangitis (q.v.) is often associated with stones, there is a *clinical picture of pain, chill, fever, and jaundice* (*Charcot's intermittent hepatic fever*). Many pathological states affect the color of the stool. The stool may be black (due to partially digested blood from a bleeding ulcer or esophageal varices), red (due to bright blood from the rectum), watery with blood and mucus (ulcerative colitis), white or acholic (obstructive jaundice), etc. The urine also varies in color: in obstructive jaundice (choluria) it is deep orange; in other types of jaundice (acholuria), it is normal in color. The *treatment for gallstones is surgical removal of the stones and the gall bladder—cholecystectomy*. Cholecystostomy (removal of stones and drainage of gall bladder) is rarely done. It is indicated in those patients who are in poor condition or in those cases with superimposed acute inflammation where because of technical difficulties cholecystectomy would be too hazardous. Cholecystectomy may then be done at a more favorable time. Stones in the common duct are removed through an incision (choledochostomy), followed by drainage. If a bile fistula persists after this operation, an overlooked stone is probably obstructing the common duct. This may be visualized by injecting Lipiodol and making an x-ray. Ether in oil has been injected to dissolve soft common duct stones with partial success; also, Albright's solution G (similar to magnesium citrate) may facilitate their passage.

It is very important that the surgeon *identify* the ducts and blood vessels. Since congenital anomalies are very common, and since acquired distortions are to be expected in the presence of disease due to inflammation, edema, dense adhesions, serious injuries may follow careless surgery. *In order to avoid injuries to the common bile duct*, some surgeons have advocated a "*high cholecystectomy*," leaving a part of the lower portion of the gall bladder. This is apt to be followed by reformation of a tiny gall bladder in which stones may reform.

The question of routine exploration of the common bile duct has been thoroughly discussed in current literature. Those who advocate it aver that otherwise stones may be overlooked. All are agreed that choledochostomy is not entirely innocuous. It is our custom to expose the cystic and common ducts routinely. The latter is carefully palpated,

gall bladder, removing all stones, and, then, by subserous dissection, removing it after carefully identifying the cystic duct and artery.

In the presence of perforation, cholecystostomy followed by drainage of the gall bladder area is the treatment of choice, because manipulations spread infection and the simplest procedure possible is done.

It is unwise to explore or even uncover the common bile duct in the presence of acute cholecystitis because the swelling and edema and adhesions make such exploration difficult and also because such maneuvers spread infection. The treatment of some of the *complications* and sequelae of acute and chronic cholecystitis should be mentioned.

Perforations causing local abscess or subphrenic abscess or empyema will require cholecystostomy and drainage of the localized accumulation of pus. Biliary branchial fistulae are best attacked transpleurally as well as through the abdomen.

Perforations causing *fistulae* into the gastrointestinal tract can be diagnosed by the history of gall stone disease and x-ray studies which may *show air in the biliary tract.* Surgery consists of separation of the gall bladder from the organ involved, cholecystectomy, and closure of the opening in the hollow viscus. If the stone has caused an intestinal obstruction, this will obviously take precedence and will be treated first (see Chapter 20).

Adhesions about the gall bladder are dissected free by sharp dissection as close to the gall bladder as possible.

Stones in the common duct should be removed. Sometimes they reform; more often some are overlooked. Their removal is done by choledochostomy. This should be done carefully and under full exposure. The incision is made longitudinally and should be large enough to permit the removal of the stone without tearing the duct. The duct should be drained with a small catheter or T tube (we prefer the former because removing the T tube is always attended by more than minimal trauma and sometimes actual tearing). Closure is made with interrupted silk sutures and may be done so as to close the opening transversely if small. Some surgeons inject Lipiodol or other opaque media through the tube and make an x-ray film before closing the abdomen to prevent overlooking a stone. The gastrohepatic ligament is sutured around the closure, and soft Penrose tubes are placed around the opening in the duct to take care of leakage.

Acute cholangitis is seen associated with "ball valve" stone in the common bile duct (Charcot's intermittent hepatic fever). Formerly a mild form was described as ascending catarrhal jaundice. It was thought that infection from the duodenum spread up a patulous duct, infecting the bile duct. This type is now thought to be due to infectious hepatitis. The most common variety of acute cholangitis follows common duct surgery, either simple exploration (choledochostomy) or, more commonly, following repair of benign strictures by excision and anastomosis, or cholecystoduodenostomy. Here again the explanation has been on the

fact that the vague pain which persists in the region of the gall bladder occurs more commonly in those cases where considerable trauma was necessary to remove the organ. This has been explained on the basis of nerve irritation which may correspond to amputation neuroma and "phantom limb" (see Chapter 6).

Inflammations of the Gall Bladder.—Usually when there are stones there are signs of chronic inflammation of the gall bladder, and occasionally there is inflammation in the absence of stones (typhoid cholecystitis, biliary ascariosis). Experimentally acute cholecystitis may be produced by injecting concentrated bile into the gall bladder or into the peritoneal cavity. Also, concentration of bile salts may produce a chemical irritation of the gall bladder. Its wall is not full of bacteria and polymorphonuclear leucocytes as in an acute infection. However, the edema and softening of the gall bladder wall as a result of chemical inflammation may permit bile to seep through the gall bladder wall, giving rise to biliary peritonitis without demonstrable perforation. However, the gall bladder is well able to cope with this situation, and it is extremely uncommon to find this organ acting as a focus of infection. This makes it possible to open the gall bladder and remove the stones without postoperative wound or peritoneal infection. Chronic inflammations of the gall bladder are common and are probably due to *chemical* causes, or if stones are present, to *mechanical* ones. Those due to *infections* are rare and are practically always associated with obstruction of the cystic duct, which interferes with the blood supply (gangrene) or impairs it sufficiently to cause infarction. Following this interference with function and blood supply due to stone impaction, the gall bladder may become inflamed (acute cholecystitis), or gangrenous, or (occasionally) filled with what appears to be pus (empyema of the gall bladder). We have made repeated cultures of this pus and found it sterile; there were some lymphocytes and a few polymorphonuclear leucocytes and mucus. Even sections of the gall bladder wall show relatively few pus cells. The entire process resembles a chemical rather than a bacterial one. Pancreatic juice is found in the gall bladder frequently and is due to the pancreatic and common bile ducts being converted into a continuous tube by spasm of the sphincter of Oddi. When the two ducts enter through the same opening, should pancreatic juice enter the gall bladder under pressure, cholecystitis may result. The reverse of this is true in pancreatitis, *q.v.* Rarely, a gall bladder, like an appendix, will rupture; incidence is about 1/4 of 1 per cent. Therefore, when a patient has pain, rigidity, and tenderness over the gall bladder area, and, in addition, has chills, fever, and leucocytosis, his course should be carefully observed by the surgeon from hour to hour. If all symptoms and signs subside, surgery is deferred to a more favorable time. If not, surgery is done, and usually it is as conservative as possible; that is, drainage of the gall bladder (cholecystostomy) after removal of the stones, although cholecystectomy may be done in selected cases, preferably by the "open method" (that is, opening the

bottom. It has been our observation that such reflux does occur as shown by ingestion of barium or Lipiodol and seeing the mixture in the biliary tract and also that it does not occur when special measures are used as described above to prevent it. Far more important, however, is the patency of the anastomosis. In the presence of a wide open junction, reflux apparently causes no trouble, whereas in those anastomoses with strictures, repeated attacks of cholangitis occur no matter what variety of anastomosis is employed. This same principle is true with ureterocolic anastomosis also.

Chronic cholangitis is seen in association with stones in the ducts and requires drainage of the common duct after choledochostomy, although drainage *down to* the duct is practiced by many surgeons (as in pyelostomy).

Obstructions of the Common Bile Duct.—These obstructions are usually due to stones within the lumen or to carcinoma of the pancreas, which causes pressure from without. Occasionally acute cholangitis may produce so much edema and swelling as to obstruct the duct. This is not a chonic state, however, and soon clears as the inflammation subsides. The common duct may be injured during an operation. If it is not properly repaired, stricture may result. In any of these cases, jaundice occurs, the stools are clay colored, and the urine assumes a deep orange color. The differential diagnosis is mentioned in the paragraphs dealing with the above causes.

The entire list of the more common causes of obstruction may be outlined as follows:

1. Congenital malformations
   a. Atresia
   b. Stenosis with thick mucus or bile
2. Gallstones
3. Trauma
   a. Injury due to severe external force
   b. Operative injury (95 per cent of all postoperative obstructions)
   c. With acute cholecystitis or its complications
   d. Pancreatitis
5. Cysts
   a. Within duct
   b. Outside duct (hydrops of gall bladder, mesenteric cyst, pancreatic cyst)
6. Neoplasms
   a. Benign
      (1) Within the duct—adenomyoma, fibroma, papilloma, polypi
      (2) Outside—hepatic, pancreatic, and mesenteric
   b Malignant
      (1) Within—carcinoma of ducts primary or by extension from gall bladder or liver; carcinoma of ampulla
      (2) Outside—carcinoma of pancreas

Stricture of the duct is difficult to cure. Usually the gall bladder has been removed and cannot be used for anastomosis. (Therefore, some advocate cholecystostomy when choledochostomy is necessary.) The duct

basis of reflux; that is, duodenal content is carried into the biliary ducts, causing repeated acute inflammations. To offset this possibility, various operative maneuvers have been suggested; namely, suturing the duct to the jejunum and anastomosing the ascending and descending loops (hepaticojejunostomy and jejunojejunostomy); the Y loop or Roux principle with and without artificially constructed valves, forming a baffle against ascending infection (valves are made by infolding all the coats of the jejunum or simply the serosa over a catheter; using special Vitallium or plastic or rubber tubes wide at the top and narrow at the

Fig. 376.—Cicatricial obstruction to the common bile duct. The x-ray photograph is that of a woman age 54 years who was operated upon elsewhere for gallstones in the gall bladder and common bile duct. Following her operation she became deeply jaundiced and developed what she termed an abscess at the site of the incision. This was opened and a prodigious amount of bile was drained. Following this procedure the jaundice disappeared but the bile continued to drain.

On entering the hospital the patient was greatly emaciated and extremely weak. She complained that she had lost her appetite, that the stools were light in color, and that the bile flowed continuously from the incision.

At operation the common hepatic duct was identified but the common duct was not present. The duodenum was mobilized and was brought up to the common hepatic duct over a Vitallium tube as shown in the x-ray photograph. The patient was greatly improved and was released from the hospital two weeks after surgery.

Eight months later she returned complaining of jaundice, chills, and fever. The patient was operated upon again and the Vitallium tube was found to be completely occluded by muddy bile and was removed. At this time the jejunum was brought up to the common hepatic duct in the manner of a Roux Y anastomosis.

She re-entered the hospital one year later stating that she had had some episodes of chills and fever. However, after a period of approximately ten days' observation she was released from the hospital and was well when last seen. This illustrates the great problem of cicatricial obstructions to the common bile duct. The use of a foreign body to maintain a patent lumen is questionable. The new plastics which are supposed to be entirely innocuous are still foreign bodies. The present method of treatment is to anastomose the ends of the common duct if this is possible and, if not, to bring up a loop of bowel to the proximal end of the duct so that there will result a mucosa-to-mucosa union. This should be done even if it is necessary to resect a part of the left lobe of the liver to get a normal duct. Then, and only then, can stricture be prevented from reforming.

appearance of being old, rather than the soft mushy variety; in cases of bile stasis as a result of carcinoma of the common duct or head of the pancreas, the incidence of stones is no greater than in the age group affected. Pathologically three types are seen. All are adenocarcinoma: the villous papillomatous or fungating type, the gelatinous type, the diffuse flat infiltrating type. The symptoms and signs are those of chronic cholecystic disease with stones. The diagnosis is difficult to make in the early stage, although occasionally the cholecystogram may arouse suspicions. In late cases with a large, hard mass in the right upper quadrant, painless jaundice, loss of weight, and anemia, it may be suspected. Usually the diagnosis is made at operation or after the gall bladder has been removed. Treatment consists of resection of the gall bladder and the adjacent liver bed, and if there is involvement of the common duct, this, too, may be removed, followed by anastomosis of the common hepatic duct with the duodenum or jejunum.

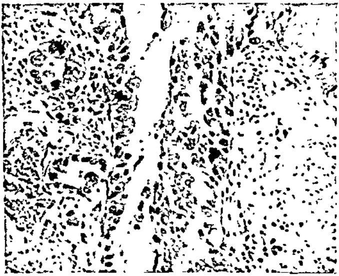

Fig. 377.—Carcinoma of the gall bladder. Note the large undifferentiated cells and their invasion of the submucosa. The gall bladder was enormously distended with a clear mucoid fluid.

Carcinoma of Extrahepatic Ducts and the Ampulla of Vater.—Carcinoma of the extrahepatic ducts is rare and of two pathological types, nodular and papillary. Both grow inward, causing early obstruction to the duct. The common duct is the most frequent site if the ampulla and papilla of Vater are included, next, the junction of the cystic, hepatic, and common, and, last, the hepatic ducts. Symptoms and signs are jaundice with complete biliary obstruction in over 90 per cent. The onset is usually sudden and may be accompanied by chills and fever, vomiting, and pain in over half the cases. Therefore, the usual diagnosis is stone in the common duct, and the true nature of the lesion is discovered at surgery. The treatment consists of resection of the duct, and if the

itself may be so fibrosed that it cannot readily be sutured. This may be facilitated by introducing into it a catheter which is allowed to protrude into the duodenum and then suturing the duct around the catheter. Another ingenious method is to transplant the fistulous tract (which is usually present) into the duodenum.

Some of the methods employed in treating strictures have been described. The principles involved are:

1. Suture of the proximal to the distal end of the duct if possible. This may be accomplished sometimes by splitting the pancreas and uncovering the distal end of the duct. This method has the advantage of preserving the sphincter.

2. Anastomosis to the duodenum or jejunum with as wide a stoma as possible in an isoperistaltic manner.

3. Mucosa sutured to mucosa to avoid stricture.

4. Foreign bodies (Vitallium, plastic tubes, rubber tubes) useful as *temporary splints*. Like all foreign bodies, they soon become obstructed or induce such reaction as to engender fibrosis unless they are passed spontaneously.

5. Division of liver substance between mattress sutures until the proximal end of a large duct is encountered or removal of a portion of left lobe of the liver using the large duct of this lobe.

6. In intrahepatic anastomoses a cuff of mucous membrane may be fashioned by removing the outer coats of the bowel. This cuff is sutured to the proximal end of the duct. The outer coats are then sutured to the liver.

Tumors and Cysts.—Common duct cysts are best *treated* by anastomosis of the cyst wall to the duodenum. We have had two cases. Wide anastomoses were made, and no cholangitis has followed. If in the gall bladder, they may be removed or treated as above.

Benign neoplasms of the common duct or ampulla are removed through choledochostomy or transduodenal resection. Usually they are diagnosed as impacted stones. When removed, they are submitted for biopsy, and if found to be malignant, more radical surgery is done. Benign neoplasms of the gall bladder are usually discovered after cholecystectomy. By careful x-ray studies they may be diagnosed preoperatively. Treatment consists of cholecystectomy.

Malignant neoplasms of the gall bladder comprise about 5 per cent of all cancers seen at post-mortem. In various reported series of surgically removed gall bladders, the incidence of the disease has ranged from 0.2 to 5 per cent. Gallstones apparently constitute an exciting factor and may, in addition to the irritative and digestive action of bile, combine to produce a susceptibility to the disease. Stones have been found in 60 to 80 per cent of all carcinomas of the gall bladder. Although they may be the result of carcinoma, this seems unlikely because there is usually a history of gallstone colic and the stones are hard and faceted, giving the

The patient complains of itching. There are bradycardia, sometimes delirium, and a marked bleeding tendency. The bleeding tendency in jaundice is thought to be due to loss of capillary tone and deficiency in prothrombin. Vitamin K (derived from liver, putrefied fish meal, and alfalfa and the action of coliform bacteria in the large bowel—intrinsic source) seems to increase the prothrombin when given with bile by

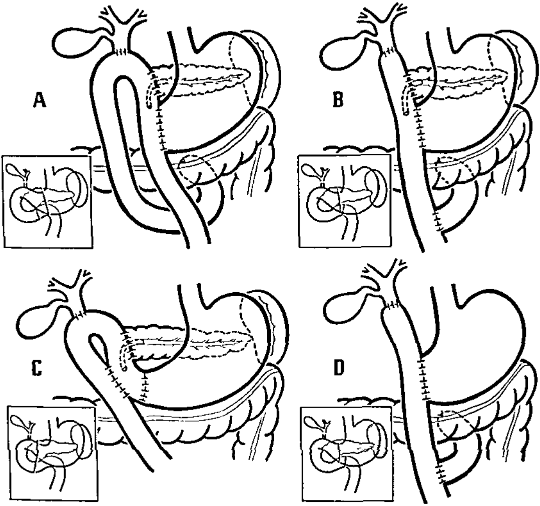

Fig. 378.—Diagrams illustrating methods of resection of the head of the pancreas and of all the pancreas Partial pancreatectomy and total pancreatectomy (Whipple). *A.* An antecolic, isoperistaltic anastomosis with a loop of jejunum. *B.* Antecolic (or postcolic) anastomosis with the Roux Y jejunojejunostomy. *C.* Resection of the head of the pancreas with a Billroth 1 type of stomach-duodenal anastomosis and, in addition, a duodenojejunal anastomosis. *D.* Total pancreatectomy, partial (or total) duodenectomy and splenectomy with Roux Y anastomosis.

mouth. The endothelioblastic or P factor in this hemorrhagic tendency is controlled by giving large doses of vitamin C (cevitamic or ascorbic acid), whereas the calcium balance may be influenced by vitamin D. Therefore, in preparing a jaundiced patient for surgery, a diet rich in protein and carbohydrate and low in fat is given to prepare the liver

gall bladder is uninvolved, it may be used to form an artificial duct by attaching the proximal end to one side of the gall bladder, then doing a cholecystoduodenostomy. If the gall bladder and cystic duct must be sacrificed, a tube may be fashioned from the jejunum much like the Janeway gastrostomy.

Ampullary carcinoma (including the ampulla of Vater and duodenal papilla) constitutes about 1½% of all carcinomas found at autopsy. Grossly there are two types, the papillary type and the ulcerating type, whereas microscopic studies will show adenocarcinoma of all varieties. The neoplasms spread by direct extension into the duodenal wall, pancreas, and common bile duct. They metastasize to nodes of the first echelon, the liver, and the lungs by lymphatic routes and also by the portal vein.

Symptoms and signs include pain which is vague and constant, jaundice which may be painless and progressive or intermittent, or painful intermittent jaundice; occasionally there are chills and fever from an associated cholangitis. Later there are loss of weight, anorexia, and anemia. The gall bladder is distended if there is no associated cholecystitis with stones. A distended gall bladder in the presence of painless jaundice suggests obstruction due to malignancy—Courvoisier's law. Laboratory studies which may help in the diagnosis include tests for occult blood in the stoools, duodenal drainage and study of the duodenal content for blood and neoplastic cells; x-ray examination may show a filling defect at the papilla or flattening or displacement or reversed **3** sign of the preampullary portion of the duodenum. The diagnosis is usually established at operation because the symptoms and signs resemble stone in the common duct, carcinoma of the head of the pancreas, carcinoma of the duodenum or extrahepatic bile ducts. The treatment consists of removal of the distal portion of the duct together with the involved part of the duodenum and pancreas followed by implantation of the common duct into the jejunum. The extent and variety of this procedure will vary with the size and position of the growth and the preference of the surgeon. Our usual desire is to do a one-stage "Whipple type" operation, consisting of resection of the common duct, first portion of the duodenum, and head of the pancreas, part or all, and then closure of distal end of the duodenum, anastomosis of the jejunum to the pyloric end of the stomach (anticolic, Polya type), and implantation of common bile duct into the jejunum (ascending loop). The pancreas is closed with interrupted silk sutures and the pancreatic duct is ligated or, if feasible, anastomosed over a small tube to the jejunum. (See Fig. 378.)

Jaundice.—The clinical state known as jaundice consists of a yellow pigmentation of the skin and is due to the deposition of bile pigment (or pigment from the disintegration of blood corpuscles) in the skin. The sclera are tinted yellow and, in jaundice of the obstructive type the urine is deeply colored due to the presence of bile. The serous cavities and parenchymatous organs may also be bile-tinged due to cholemia.

b. Causes in the wall of the ducts
  (1) Inflammation (cholangitis)
  (2) Strictures
  (3) Congenital anomalies (atresias and stenosis)
  (4) Benign and malignant neoplasms in the ducts or ampulla
c. Causes outside the ducts
  (1) Carcinoma at the head of pancreas
  (2) Carcinoma of the duodenal papilla
  (3) Tumors and cysts pressing on ducts
  (4) Lymphadenopathy at the hilus
  (5) Chronic pancreatitis
  (6) Cysts of the pancreas

The cause of the jaundice is an increase in the intrabiliary pressure with a rhexis of the ampullary portions of the small bile capillaries, permitting posthepatic bile to be absorbed by the liver lymphatics. There is also leakage without actual rupture of the bile capillaries which become more permeable as they dilate. The bile capillaries also become more permeable as a result of toxic agents and anoxemia, permitting bile leakage.

Intrahepatic jaundice or jaundice due to hepatocellular damage (toxic or infective) is due to a destruction of liver cells by some disease such as *acute yellow* atrophy of the liver or by poisons which affect the liver cells, such as chloroform, or toxins from bacteria, or virus infections. In this case some bile may be present in the stools, the urine will contain large quantities of bile, the liver will be markedly enlarged, and no symptoms of obstruction as previously described will be present, although when hepatocellular damage is extensive, the stools may be acholic and the urine may contain very little urobilinogen. Since there is some hepatocellular damage in all types of jaundice, particularly the obstructive variety, it is possible to classify the intrahepatic type of jaundice with precision. The causes, therefore, must include those mentioned under obstructive jaundice and, in addition, epidemic hepatitis, homologous serum jaundice, poisons (carbon tetrachloride, chloroform, phosphorus, phenylhydrazine, arsenic, cinchophen, the sulfonamides), epidemic jaundice, Weil's disease (Chapter 7), hyperthyroidism, eclampsia, severe or prolonged hematogenous jaundice, yellow fever, the cirrhosis, carcinoma, lymphosarcoma, the leucemias.

Hemolytic or acholuric jaundice has nothing to do with the liver per se but is due to a dissolution of red blood cells in large numbers with disintegration of the hemoglobin and deposition of the pigments in the skin. This condition is diagnosed by the fragility test of red blood cells, the presence of abnormal cells such as the spherical microcyte of congenital hemolytic arteries, the sickle cell in sickle-cell anemia, the variation in types and numbers of white cells in the leucemias. The urine contains no bile as a rule. Since about half or the cases of congenital hemolytic jaundice have stones, there may be an obstructive jaundice as well. It is associated with splenomegaly and is treated sometimes by splenectomy.

for the ordeal (since the crippled liver may not be able to store glycogen). Blood transfusion, vitamin K with bile, and vitamins C and D should also be a part of the preoperative prepartion. (Vitamin K is now produced synthetically and may be given parenterally without bile.) Other symptoms and signs depend upon the causative factors. We have discussed previously the physiology of bile formation, excretion, and absorption; also, the difference between pre- and posthepatic bile. Function tests and methods which help in evaluating liver reserve and the probable cause or causes of jaundice have also been mentioned. It remains now to classify the types of jaundice as to their cause, to evaluate symptoms and signs in an effort to make the proper diagnosis, and to institute the correct treatment.

In general, there are three causes for jaundice: excessive hemolysis, destruction of liver cells, and obstruction of the duct system, although any two or all three causes may be present at the same time; that is, jaundice may be due to (1) the production by the reticulo-endothelial system of more bile pigment than the liver can excrete (as in hemolytic jaundice and malaria), (2) inability to excrete a normal amount of bile because of liver damage (as in cardiac decompensation and Hanot's cirrhosis), or (3) failure to eliminate the bile which is secreted because of obstruction.

The first two conditions produce *retention* jaundice; bilirubin is held back, which may be suspected by the fact that the serum gives an *indirect* van den Bergh reaction. The third condition produces *obstructive* jaundice (or regurgitation jaundice) and may be due to calculi, inflammation, neoplasms, stenosis, or necrosis of liver cells. Bilirubin is secreted by the liver cells but because of the obstruction cannot be excreted. In this condition the blood serum gives a *direct* van den Bergh reaction (just as bile itself does) and the urine contains bilirubin.

Obstructive jaundice is due to a blockage of the common bile duct. This may be due to obstruction within the duct, as in the case of a stone, or to obstruction caused by extraneous pressure, as in carcinoma of the head of the pancreas (as will be pointed out in the following section). The stools will be white in color. The causes of obstructive jaundice may be classified as follows:

1. Obstruction of bile ducts in the liver
   a. Partial
      (1) Inflammatory lesions such as amebic, pyelephlebitic, and pyemic abscesses; cholangitis
      (2) Early biliary cirrhosis
      (3) Tumors and cysts, such as carcinoma, primary or metastatic, echinococcus cysts
   b. Total or almost total
      (1) Late biliary cirrhosis
2. Obstruction of bile ducts outside the liver
   a. Causes within the ducts
      (1) Stone
      (2) Papilloma
      (3) Carcinoma

The alveoli of the gland develop as dark-staining buds in 45-day embryos, and the islands do not appear until about 60 to 70 days.

The main arterial supply is from the gastroduodenal artery, a branch of the hepatic from the celiac artery. The gastroduodenal descends between the duodenum and pancreas and divides into the right gastroepiploic and the superior pancreaticoduodenal. The pancreas also receives blood from the inferior pancreaticoduodenal artery, a branch of the superior mesenteric artery, or one of the jejunal branches, and the pancreatic rami from the splenic. The veins are the pancreatic duodenal and small branches which empty into the splenic. The lymph vesels empty into the celiac nodes as well as the superior mesenteric chain. The nerves are now medullated and come from the celiac, hepatic, and splenic plexuses.

From this discussion, it may be understood how some of the pancreatic variations and anomalies may occur. Among these are the following: (1) Duplication. The uncinate process may be entirely separate, forming a lesser pancreas. (2) Overdevelopment of the uncinate process, converting the letter J, which lies thus ⊂ normally, to the letter U, lying thus C. This is important in pancreatic resections. (3) Annular pancreas which completely surrounds the duodenum and which may cause an obstruction. (4) The pancreatic duct may open into the duodenum separate from the common bile duct in 20 per cent of people; in 20 per cent they form a common channel of some length; in 60 per cent they empty together in the ampulla. (5) Accessory pancreas may be found in the wall of the stomach or duodenum, or heterotopias may be found in Meckel's diverticulum or parts of the gastrointestinal tract. (6) Duodenal diverticula may, in fact, be remnants of the outpouchings which give rise to the liver and pancreas.

The pancreas is located in the upper posterior portion of the abdomen in what is roughly described as the epigastric region. The organ lies against the spinal column and is covered by a layer of visceral peritoneum (on its inferior surface) and by the bursa omentalis (on its anterior surface). Anterior to the pancreas is the lesser peritoneal cavity, which, as we have learned, is bounded anteriorly by the stomach, on the right by the gastrohepatic ligament, and on the left by the gastrosplenic ligament. There is one opening between the lesser and the greater peritoneal cavity known as the foramen of Winslow, or the gastroepiploic foramen. It may be readily understood, then that the pancreas (even when diseased) is not readily palpable because of the deep situation of the organ and the fact that the stomach lies anterior to it.

The pancreas elaborates an external secretion (pancreatic juice) and, in addition, an internal secretion (insulin), which has to do with sugar metabolism. The external secretion flows through the pancreatic duct (duct of Wirsung, and the accessory pancreatic duct (duct of Santorini) and enters the duodenum. (Usually the pancreatic duct empties at the ampulla of Vater with the common bile duct, but often the ducts empty separately.) The pancreatic juice contains amylase (or amylopsin or diastase), which digests carbohydrates, lipase (or steapsin), which digests fats, trypsin, which digests protein, rennin, which has an action similar to that of gastric rennin, and maltose in small amounts (see Chapter 20).

The internal secretion, insulin, is elaborated by the islands of Langerhans and metabolizes sugar. This secretion is hormonal, for it is carried by the blood stream, and when it is absent or decreased, *diabetes mellitus* results. *Diabetes mellitus* is also intimately related to the pituitary secretion (diabetogenic factor). Houssay has shown that diabetic symptoms following pancreatectomy almost disappear after hypophysectomy. Dogs die after pancreatectomy unless treated with insulin. If, however, the hypophysis is removed, symptoms disappear.

Total pancreatectomy in man requires only small amounts of insulin. In fact, the depancreatized man requires less insulin and is more sensitive to insulin than many diabetic patients, a fact which makes one think that diabetes mellitus

The causes of *hematogenous* jaundice include severe infections with septicemia or bacteriemia (see Chapter 5), malaria, pernicious anemia, icterus neonatorum, high gastrointestinal or internal hemorrhage, erythroblastosis fetalis, familial hemolytic icterus, sickle-cell anemia, hemolytic transfusion reaction, hemolytic poisons or allergens. As we review the respective causes, we see that they are interrelated and more than one factor may be acting simultaneously. Thus a patient with obstructive jaundice and liver damage may have extensive internal hemorrhage (all three types) or severe anemia, hepatic anoxia, and thick bile, causing an obstruction (again all three types). Such combinations occur commonly in yellow fever, spirochetal disease, erythroblastosis fetalis, hemolytic icterus, and after administration of the hemolytic-hepatotoxic drugs such as arsphenamine, phenylhydrazine, etc.

The diagnosis of the type of jaundice depends on an accurate history, careful study of all symptoms and signs, and laboratory aids.

The treatment depends upon the cause. The greatest problem is not the medical management of the jaundiced patient, but the decision as to whether or not surgery is indicated. It is indicated in the obstruction types—gallstones, bile fistulae, complete and permanent obstruction from carcinoma. It is not indicated in primary hepatocellular types. Thus, a history of blood or plasma transfusions within recent months, or the taking of certain drugs as mentioned, the presence of collateral circulation or vascular spiders or edema lead one to think in terms of nonsurgical jaundice. Severe jaundice with bile in the stools usually means diffuse hepatocellular (intrahepatic) jaundice, and if, in addition, the prothrombin time is not shortened by the administration of vitamin K, the damage is probably widespread.

The Pancreas

The pancreas develops from two anlages which appear in 3 to 4 mm. embryos about the same time. The *dorsal pancreas* arises as a pouch from the posterior wall of the duodenum just above the diverticulum. It grows in the greater omentum between the duodenum and stomach, where its distal portion is constricted to form the accessory pancreatic duct, and its main portion takes part in forming the head and uncinate process and makes up the whole of the body and tail. The *ventral* pancreas develops in the angle between the hepatic diverticulum and the duodenum, and with the development of the bile duct it becomes separated from the duodenum, although it may arise directly from the wall of the duodenum. The ventral pancreas is much smaller, and it gives rise to the main pancreatic duct which enters into the common bile duct and forms part of the head and uncinate process. Ultimately the two ducts unite and the duct of the dorsal pancreas becomes the accessory duct (Santorini), whereas the duct of the ventral becomes the functional pancreatic duct (Wirsung).

In 35-day embryos the portal vein separates the two pancreatic anlages, and later they partially surround the vein. The superior mesenteric vein thus passes through the pancreas and is joined by the splenic vein which runs along the posterior surface of the pancreas, receiving small veins from the organ. As the stomach and duodenum rotate to the right, the pancreas takes a transverse position with its tail to the left, and the transverse mesocolon comes to be anterior to it. The gland has no true capsule.

The alveoli of the gland develop as dark-staining buds in 45-day embryos, and the islands do not appear until about 60 to 70 days.

The main arterial supply is from the gastroduodenal artery, a branch of the hepatic from the celiac artery. The gastroduodenal descends between the duodenum and pancreas and divides into the right gastroepiploic and the superior pancreaticoduodenal. The pancreas also receives blood from the inferior pancreaticoduodenal artery, a branch of the superior mesenteric artery, or one of the jejunal branches, and the pancreatic rami from the splenic. The veins are the pancreatic duodenal and small branches which empty into the splenic. The lymph vessels empty into the celiac nodes as well as the superior mesenteric chain. The nerves are now medullated and come from the celiac, hepatic, and splenic plexuses.

From this discussion, it may be understood how some of the pancreatic variations and anomalies may occur. Among these are the following: (1) Duplication. The uncinate process may be entirely separate, forming a lesser pancreas. (2) Overdevelopment of the uncinate process, converting the letter **J**, which lies thus ⊂ normally, to the letter **U**, lying thus **C**. This is important in pancreatic resections. (3) Annular pancreas which completely surrounds the duodenum and which may cause an obstruction. (4) The pancreatic duct may open into the duodenum separate from the common bile duct in 20 per cent of people; in 20 per cent they form a common channel of some length; in 60 per cent they empty together in the ampulla. (5) Accessory pancreas may be found in the wall of the stomach or duodenum, or heterotopias may be found in Meckel's diverticulum or parts of the gastrointestinal tract. (6) Duodenal diverticula may, in fact, be remnants of the outpouchings which give rise to the liver and pancreas.

The pancreas is located in the upper posterior portion of the abdomen in what is roughly described as the epigastric region. The organ lies against the spinal column and is covered by a layer of visceral peritoneum (on its inferior surface) and by the bursa omentalis (on its anterior surface). Anterior to the pancreas is the lesser peritoneal cavity, which, as we have learned, is bounded anteriorly by the stomach, on the right by the gastrohepatic ligament, and on the left by the gastrosplenic ligament. There is one opening between the lesser and the greater peritoneal cavity known as the foramen of Winslow, or the gastroepiploic foramen. It may be readily understood, then that the pancreas (even when diseased) is not readily palpable because of the deep situation of the organ and the fact that the stomach lies anterior to it.

The pancreas elaborates an external secretion (pancreatic juice) and, in addition, an internal secretion (insulin), which has to do with sugar metabolism. The external secretion flows through the pancreatic duct (duct of Wirsung, *and the accessory* pancreatic duct (duct of Santorini) and enters the duodenum. (Usually the pancreatic duct empties at the ampulla of Vater with the common bile duct, but often the ducts empty separately.) The pancreatic juice contains amylase (or amylopsin or diastase), which digests carbohydrates, lipase (or steapsin), which digests fats, trypsin, which digests protein, rennin, which has an action similar to that of gastric rennin, and maltose in small amounts (see Chapter 20).

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is due not only to too little insulin, but to an insulin-inhibiting mechanism as well, although there is no proof for the latter. The depancreatized human being requires about 40 to 70 units of insulin daily during the first week, and can be maintained on 25 to 40 units daily thereafter.

Depancreatized dogs receiving insulin and a diet of meat and carbohydrates develop fatty livers unless raw pancreas is added to the diet. Lecithin, choline (a base in the lecithin molecule), the amino acid methionine, which gives its methyl group to aid in the formation of choline, and *lipocaic* (Dragstedt), a pancreatic hormone, also prevent the formation of fatty livers in depancreatized dogs. In addition, dogs without a pancreas lose about 50 per cent of the fat and about 20 per cent of the carbohydrate in their stools.

This work is now of great practical importance because it provides a scientific basis for maintaining the depancreatized patient. To prevent a fatty liver and hypolipemia, readily available lipotropic substances are given such as choline (one egg yolk contains 0.5 Gm. of choline; it is also found in liver and may be given as choline chloride). Lipocaic and choline may be given by adding raw pancreas to the diet; also pancreatin, which will also reduce the loss of nitrogen and fat.

It remains to be seen whether the degenerative complications of diabetes such as diabetic arteriosclerosis, retinopathy, neuropathy, and intercapillary glomerulosclerosis) will occur after pancreatectomy in man.

Hypoglycemia.—We have just considered the cause or causes of hyperglycemia due to insufficient insulin. This is diabetes which, if untreated, does not provide for proper sugar metabolism, and the parenchymal cells of the liver as well as the cells of other tissues receive an insufficient supply of sugar, and glycogen will not be stored in them or in the liver. Hypoglycemia due to too much insulin as well as other causes provides for sugar metabolism at such a fast rate that again the liver cells cannot store glycogen nor can the tissue cells utilize it. The causes of hypoglycemia may be (1) hepatogenic, (2) organic hyperinsulinism, (3) functional hyperinsulinism. A more detailed outline has been arranged by Conn:

Etiologic Classification of Spontaneous Hypoglycemia

I. Organic—recognizable anatomic lesion
  A. Hyperinsulinism
    1. Pancreatic island cell adenoma
      (a) Single
      (b) Multiple
      (c) Aberrant
    2. Pancreatic island cell carcinoma
      (a) Localized
      (b) With metastases
    3. Generalized hypertrophy and hyperplasia of the islands of Langerhans
  B. Hepatic disease
    1. Ascending infectious cholangiolitis
    2. Toxic hepatitis
    3. Diffuse carcinomatosis
    4. Fatty degeneration or "fatty metamorphosis"
    5. Glycogenosis (von Gierke's disease)
  C. Pituitary hypofunction (anterior lobe)
    1. Destructive lesions (chromophobe tumors, cysts)
    2. Atrophy and degeneration (Simmonds' Disease)
    3. Thyroid hypofunction (? secondary to pituitary hypofunction)

D. Adrenal hypofunction (cortex)
    1. Idiopathic cortical atrophy
    2. Destructive infectious granulomas
    3. Destructive neoplasms
E. Central nervous system lesions (hypothalamus or brain stem; interference with nervous control of blood sugar)

II. Functional—no recognized anatomic lesion but explainable on basis of unusual somatic function
A. Hyperinsulinism (imbalance of the autonomic nervous system): hypoglycemic fatigue, nervous hypoglycemia, functional hypoglycemia, reactive hypoglycemia
B. Alimentary hyperinsulinism (rapid intestinal absorption)
    1. After gastroenterostomy
    2. After gastric resection (partial or total)
C. Renal glycosuria (severe degrees of low renal threshold for dextrose)
D. Lactation
E. Severe continuous muscular work

III. Miscellaneous
A. Factitious (surreptitious insulin administration)
B. Postoperative hypoglycemia
C. Severe inanition
D. Unknown

The various causes for hypoglycemia are important to remember because upon proper diagnosis depends the treatment. Although glycogen is found in many tissues of the body, the fact that fatal hypoglycemia always follows hepatectomy is sufficient evidence that the liver is the main source. Glucose or those substances which may be converted to glucose without the aid of the liver are the only remedies which will prevent death from hypoglycemia in the liverless animal. The cause of death from hypoglycemia may be due to functional alterations in the central nervous system. Glucose is the main, if not the only, source of energy for the brain. It would appear that the cause of death in hypoglycemia, no matter what its cause may be, is the same; namely, an interference with oxidative metabolism of the brain. The cerebral hemispheres are affected first and then the vital centers in the medulla. Thus glucose is as necessary for life as is oxygen, and when the blood sugar gets below a certain critical level, symptoms will occur which are characteristic, and death will follow if the condition is not alleviated.

The usual symptoms of hyperinsulinism as defined by Whipple (Whipple's triad) and which usually indicate organic disease are (1) disorders of the central nervous system such as confusion, coma, convulsions, collapse coming on in a fasting state, (2) a drop in the blood sugar level to 50 mg. per 100 c.c. or less, (3) relief of symptoms brought about by the administration of glucose.

The possibility of a spontaneous hypoglycemia must be kept in mind so that erroneous diagnosis will not be made (epilepsy, intracranial tumor, narcolepsy psychosis, psychoneurosis, peptic ulcer, etc.). Moreover, in a given case of hypoglycemia, the differential diagnosis may be difficult. Certain tests are helpful: (1) a fasting blood sugar below 50 mg. per 100 c.c. usually means organic hypoglycemia; (2) dextrose tolerance test (low curve); (3) liver function tests; (4) progression of symptoms clinically and lowering of blood sugar as the disease progresses means either hyperinsulinism or liver disease. (5) A diet low in carbohydrate (50 Gm. or less) and high in protein may relieve the attacks (due to the fact that while 50 per cent of the protein may yield dextrose, the slow even rate of conversion as well as the slower absorption of protein will prevent quick and great elevations in blood sugar and thereby prevent stimulation of the pancreas).

In the absence of extrapancreatic causes for hypoglycemia with low blood sugar during symptoms which are relieved by administration of dextrose, with repeated fasting blood sugars of 50 mg. per 100 c.c. when the patient has been on an adequate diet, and with depression of the fasting blood sugar below 40 mg. per 100 c.c. by carbohydrate restriction, a diagnosis of organic hyperinsulinism may be made and exploration done. The more severe and rapidly progressive the symptoms, the more apt the possibility of malignancy rather than an adenoma as a cause. Apparently the size of the carcinoma or adenoma is not necessarily commensurate with the degree of hyperinsulinism. In severe cases of hyperinsulinism where no tumor has been found, partial pancreatectomy is indicated. Apparently alloxan does not control the symptoms in human beings.

Severe postoperative hypoglycemia may occur from (1) the utilization of glucose faster than it is being supplied, (2) an insufficient amount given, (3) failure of the intrinsic hepatic mechanisms for storage, synthesis, or secretion of glucose, (4) primary hepatic insufficiency. In this discussion we are interested in (1). Any one of the conditions mentioned in the outline may be the cause or any combination may occur. In postoperative stupor, coma, or other central nervous system dysfunction hypoglycemia must be considered as a cause for the symptoms.

Tests of Pancreatic Function.—Experimental obstruction of the pancreatic duct causes a rise in blood amylase and lipase. Morphine is said to increase resistance in the sphincter of Oddi from the normal (about 150 mm. of water) to higher levels (about 250 to 300 mm. of water) causing pancreatic reflux. Normally a small amount of lipase and amylase are present in the blood stream, but not trypsin. This may mean that the former are, in part, an "internal secretion," but whether they enter the blood stream directly from the acinar cells or indirectly from the gastrointestinal tract is not known. It is thought that in inflammations the former is true because the rise in serum amylase is prompt. However, the enzymes may enter the blood stream as a result of rupture of small pancreatic canaliculi, permitting the lymphatics to carry the pancreatic juice directly into blood vessels. It is possible that inflammations of acinar cells cause a hypersecretion, whereas destruction decreases the secretion. Serum amylase may be quickly determined and varies between 80 to 180 mg. per 100 c.c. (Somogyi method), or when iodine is used to measure the rate of disappearance of starch, 300 to 350 units are considered normal. Urine amylase is also quickly measured. Serum lipase determination requires about twenty-four hours. The normal value is 1.5 c.c. of twentieth normal sodium hydroxide per cubic centimeter of serum using the method of Cherry and Crandall (olive oil is used as the substrate, and lipolytic activity is expressed in terms of c.c. n/20 Na OH liberated in 1 c.c. of serum). Elevated amylase values occur within a few hours after the onset of inflammation and reach a maximum in twenty-four to forty-eight hours. Elevated values of lipase also occur early and persist for a much longer period and are more apt to be associated with malignant disease.

Analysis of duodenal content and stools for pancreatic enzymes may give valuable information. Also, analysis of stools for undigested and unabsorbed foods in the cases where no pancreatic juice is present will show a decided increase in the quantity of fat, nitrogen, starch, and the total carbohydrate eliminated in the feces.

Tests for disturbed secretion of insulin include the examination of urine for glycosuria which may be present in acute pancreatitis and examination of the blood for hyperglycemia which may also occur in acute pancreatitis as well as in diabetes mellitus.

The pancreatic hormone concerned with fat metabolism is thought to be lipocaic. It is also believed that the alpha cells of the islands of Langerhans secrete the substance which, when excluded, leads to hypolipemia and fatty metamorphosis with impaired liver function diminished excretion of dextrose, and great sensitivity to insulin. In such cases the disturbed fat metabolism may be discovered by blood cholesterol studies and the disturbed liver function by liver tests as previously described in this chapter.

Functional Diseases of the Pancreas

Pancreatic insufficiency may occur in infancy. Fibrocystic disease or pancreatic fibrosis of the pancreas may be congenital and even familial. Either the infant dies of malnutrition or he develops pulmonary infection with fibrosis, bronchiectasis, and patchy atelectasis and may succumb before he reaches the age of adolescence. The pancreas shows the acinar tissue to be replaced by fibrous tissue or fat.

Obstructive conditions in the pancreas in the fetus are associated with meconium ileus after birth and later with nutritional disturbances in which celiac syndrome and respiratory disease predominate. The obstruction is thought to be tenacious mucus or inspissated secretion in the acini and dilated ducts, resulting in parenchymal atrophy. In children who survive more than a few months after birth both lungs nearly always show effects of obstruction in the trachea, the bronchi, and bronchioles by thick tenacious mucoid and mucopurulent material (Farber). The mucous glands of the trachea, bronchi, esophagus, duodenum, gall bladder and jejunum are distended with mucoid material. The liver resembles the pancreas in these cases.

Achylia pancreatitis may be purely functional or it may have as its background partial fibrotic changes. The exclusion of pancreatic juice from the intestine results in impairment of digestion and absorption of protein, fat, and carbohydrate. Patients lose weight and strength and have frequent bulky stools which show an excess of fat and nitrogen. Substitution therapy (pancreatin) helps in relieving symptoms and restoring health. Indeed it may be a therapeutic test as to the accuracy of diagnosis.

Pancreatic pain is due to (1) visceral impulses by way of the celiac ganglion, causing girdle pain around the mid-abdominal region and radiating in a diffuse way to the lower abdomen and (2) somatic impulses which occur when the peritoneum is stimulated. Since the peritoneum covers the body and tail of the pancreas, lesions involving this part of the organ are notorious for their severe pain carried by sensory fibers in the lower intercostal and upper lumbar nerves and extending down into the groins (ilioinguinal and iliohypogastric nerves).

The cause of pain may be inflammatory (acute and chronic pancreatitis, acute pancreatic edema, calcareus pancreatitis) or neoplastic (carcinoma, especially of the tail of the pancreas).

The treatment consists in a direct attack on the primary cause of the pain. If this is not feasible or if pain persists after pancreatic resection, unilateral (or bilateral) splanchnic nerve section and lower dorsal sympathectomy may be indicated.

Congenital Anomalies of the Pancreas

Congenital abnormalities have been enumerated under the discussion on embryology of the pancreas. Cystic fibrosis of the pancreas has been described. Although its etiology is not definitely known, it seems that

one component of the syndrome (atresia of the pancreatic ducts) is due to a congenital malformation; the other theories as to its cause (inflammation of the pancreas during fetal life and vitamin A deficiency during life) are not.

Pancreatic heterotopia, pancreatic dystopia, or **heterotopic pancreatic tissue** is not, strictly speaking, an anomaly of the pancreas itself or its blood supply but rather the presence of pancreatic tissue outside its normal location. The heerotopias are usually single and may include all components of the normal pancreas or pancreas without the islands of Langerhans. The presence of these heterotopias may mimic benign growths (adenomyoma, fibroma, leiomyoma) or carcinoma of the viscus involved. A few cases of hypoglycemia have been traced to such aberrant pancreases either because of islet-cell adenoma or carcinoma or merely hyperplasia. Furthermore, such tissue may undergo pathological changes similar to the pancreas itself (inflammation, new growths, cysts, hemorrhage, and necrosis).

Heterotopias are usually found in the stomach or duodenum but may occur in the jejunum or transverse colon or in the gastrocolic omentum or transverse mesocolon and ileum in a Meckel's diverticulum. When symptoms occur which resemble organic disease of the gastrointestinal tract, the possibility of heterotopia of the pancreas should be considered. X-ray studies may reveal the defect. If the symptoms are acute, resembling appendicitis, or if intussusception is present as a result of heterotopia, the diagnosis will be made at operation. Surgery consists of removing the tissue together with the involved segment of intestine or stomach.

Annular pancreas has been mentioned previously. The ring of pancreatic tissue may cause obstruction in the duodenum. This condition cannot be diagnosed as such prior to operation. However, the site of the obstruction may be ascertained by x-ray studies and clinical symptoms and signs (see Chapter 20). The condition is best treated by short circuiting around the obstruction by gastrojejunostomy or duodenojejunostomy.

We have recently encountered two cases of annular pancreas. One was associated with malrotation of the mid gut. Both were successfully treated by duodeno-jejunostomy, and in one the duodenum was released by dividing adhesions to the lateral abdominal wall.

Injuries of the Pancreas

Injuries to the pancreas are usually suspected in penetrating or perforating wound of the upper abdomen. However, the pancreas may be injured by direct trauma to the abdomen without external wound, and this type of injury may account for the pancreatitis which is apt to follow. The treatment of penetrating and perforating wounds is surgical. Usually the stomach or transverse colon or other organs will be injured in the line of the bullet or sharp object. All wounds are closed. If the pancreas has been penetrated, drainage is indicated because the

apparently small wound may slough and leakage may occur. Contusions to the abdomen with injury to the pancreas may give rise to symptoms and signs resembling pancreatitis. Surgery is not indicated if there has been no ruptured hollow viscus or solid organ.

Diseases and Inflammations of the Pancreas

Pancreatic calculi are rare, occurring about once in 2,000 cases seen at autopsy. Yet minor degrees of calcification within the gland are probably common. The cause of the disease is unknown. However, many theories have been advanced. (1) Calcification may be caused by the reflux of bile into the pancreas. (2) Since the stones are made almost entirely of calcium carbonate and calcium phosphate and since these salts are not normal constituents of pancreatic juice, the calculi are due to an alteration of the pancreatic secretion caused by infection (by way of the blood, lymph, or ducts). (3) Pancreatitis may give rise to calcification in the areas of necrosis which, like any infection, may heal by fibrosis or calcification—these are not calculi but may enter the ducts like the broncholiths which also occur as a result of calcifications in the lung.

Pathology.—Pancreatic calculi are like salivary calculi, being white in color and hard and rough and vary greatly in size. Rarely are they found as a solitary stone. Often there are several hundred which may be in the head (usually) or tail or all of the gland. Fibrosis is frequently present as is cystic degeneration or dilatation of the obstructed ducts. In this regard the organ resembles fibrocystic disease in infants which is due to blockage by inspissated secretion or mucus instead of calculi. Associated pathology includes large cysts, abscesses, carcinoma, or hemorrhage due to erosion of a stone into a large vessel. Sometimes the stone becomes lodged in the ampulla, giving rise to jaundice and changes in the liver if long continued (Charcot's biliary cirrhosis). In advanced stages fatty changes occur in the liver due to interference with lipocaic production. Over 35 per cent of patients with pancreatic calculi have diabetes. Pain in the upper abdomen in patients with diabetes may mean calculi in the pancreas.

The association of pulmonary tuberculosis in many of these cases may be due to the loss of weight and strength caused by achylia pancreatica due to stones in the duct. It is true that digestion is impaired and that there may be diarrhea or pale, frothy, bulky stools with undigested fat and meat, yet tuberculosis is often found without this syndrome.

Pancreatic abscess may precede the formation of stones. We have seen two cases of this kind in children: One, a girl 11 years old, later developed extensive calcification after the abscess had been drained and also pulmonary tuberculosis, from which she ultimately succumbed. The other, a boy 10 years of age, has not been heard from recently but was well five years after drainage. Rarely, other calculi are present in the bile ducts or kidneys. Hyperparathyroidism may also be present.

Symptoms.—Pain is the most common symptom but may vary from an occasional twinge to severe colic, requiring morphine. Some patients are asymptomatic. The pain is in the midline and radiates to the left upper quadrant, left back, and scapular region. There is nausea and vomiting and weight loss. Many of these patients are alcoholics or barbiturate addicts because of pain. The pain resembles that of gallstone colic or renal colic. The frequent association of diabetes and jaundice makes the diagnosis difficult. The age varies, but usualy pancreatic calculi are seen in the third or fourth decade. There are few signs. A mass may be felt if there is a cyst or extensive swelling. Laboratory studies may show elevated lipase, hyperglycemia, or glucose tolerance curves characteristic of diabetes. X-ray studies constitute the best diagnostic aid. Films should be taken in the anteroposterior, lateral, and oblique views, and since the stones are composed of calcium, they throw a dense shadow. They may be confused with renal calculi, gallstones, calcified lymph nodes, and phlebolites.

Treatment consists of dietary management and pancreatin if no pain is present or if no associated disease is noted. Otherwise surgery is indicated. The procedure most likely to give permanent relief is partial or total pancreatectomy, and this should be done where feasible. If not, the pancreatic duct may be ligated so that atrophy of the gland will take place in the acini but probably not in the island of Langerhans. An indirect method of attacking the problem is the amelioration of pain by dividing the autonomic fibers as described under Functional Diseases of the Pancreas in this chapter. Transthoracic resection of the thoracic sympathetic ganglia (third to twelfth) and of the great splanchnic nerve on one side will give relief. If the pain is in the midline, the right side is treated; if on the left, the left side is treated. Bilateral subdiaphragmatic splanchnicectomy has also been advocated. It may be done transabdominally so that exploration of the pancreas may be carried out.

Pancreatitis may be acute or chronic. The *acute* varieties may be subdivided into (1) fat necrosis, (2) hemorrhage or "pancreatic apoplexy," (3) acute hemorrhagic pancreatitis or acute hemorrhagic necrosis, (4) acute interstitial or acute parenchymatous pancreatitis, or acute pancreatic edema, (5) acute secondary pancreatitis due to perforated peptic ulcer, purulent peritonitis of lesser peritoneal cavity, acute pancreatitis as a result of pyemia, (6) virus pancreatitis associated with mumps or epidemic parotitis.

Fat necrosis is a fat tissue necrosis in the pancreas, omentum, mesentery, abdominal wall, and, rarely, the liver and subcutaneous fat. It is seen in hemorrhage of the pancreas, obstruction of the ducts by stones, trauma, acute hemorrhagic pancreatitis, and any condition which liberates lipase, splitting the fat, and, trypsin, digesting cellular tissue.

Hemorrhage is seen in passive congestion with general passive hyperemia in which there are small areas of bleeding and in pancreatic necrosis

from any cause in which a large vessel is eroded, causing extensive bleeding. Sudden death, "pancreatic death," may occur in the latter instance.

Of the inflammations of the pancreas, *acute hemorrhagic pancreatitis* is perhaps the most alarming. It has been called acute hemorrhagic pancreatitis because the activated ferment, *trypsin*, digests the pancreas, causing hemorrhage and leakage of other ferments into the general peritoneal cavity. The cause of this is thought to be the reflux of bile into the pancreas under pressure, due to closure of the sphincter of Oddi by stones or spasm (as seen in those who overeat). Mallet-Guy and co-workers have produced the disease experimentally by electrical stimulation of the greater splanchnic nerve. *Steapsin* needs no activation and readily digests peritoneal and omental fat, causing "fatty necrosis," although some observers believe that intestinal juices or tissue kinases are needed. Bile in the peritoneal cavity may produce fat necrosis by affecting tissue permeability, allowing the escape of pancreatic juice. Pathologically, this condition is characterized by little soap deposits (calcium plus fatty acids) in the fatty tissues of the abdomen.

Clinically, it is characterized by very great pain, vomiting, and often shock, with tenderness and rigidity of the upper abdomen. There is perhaps no disease except mesenteric thrombosis with as much pain. The cause has been attributed to gall bladder disease, but this is not certain.

Most patients are obese and middle-aged, although no age group is excluded. Either sex is affected and the disease is usually seen in those who have within an hour or two indulged in a heavy meal with liberal amounts of alcohol.

Acute parenchymatous pancreatitis (acute pancreatic edema, acute interstitial pancreatitis) is the most common form of acute pancreatic disease. It is a much milder condition pathologically and clinically and resembles gallstone colic or acute cholecystitis. The pathological reaction of the pancreas in acute inflammations of any kind is due to the activation of *trypsinogen to trypsin, producing edema, necrosis, and hemorrhage.* Once the process begins, it may be self-perpetuating, even though the original cause has been removed. The amount of damage depends on the amount and concentration of the enzymes in the juice which escapes. As a result of this, the damage may vary from a transient edema to necrosis of all tissue, including blood vessels with resultant hemorrhage. Secondary infection may supervene, producing *pancreatic abscess.* The presence of shock depends also on the amount of destruction and the rapidity with which it occurs. Shock may be due to hemorrhage, the presence of autolyzed tissue in the retroperitoneal and peritoneal spaces, chemical peritonitis, and reflex neurogenic factors.

The necrotic tissue may liquify, giving rise to *pseudocysts*, or it may be absorbed with resultant fibrosis or calcification or both. There will be some regeneration of glandular tissue. Extreme fibrosis, with some pseudo-

cysts, hemorrhagic cysts, necrotic suppurations, and retention cysts due to distortion or occlusion of pancreatic ducts may remain, giving rise to chronic pancreatitis.

We may summarize the two principal types of acute pancreatitis as follows:

ACUTE HEMORRHAGIC PANCREATITIS	ACUTE PARENCHYMATOUS PANCREATITIS; ACUTE INTERSTITIAL PANCREATITIS; ACUTE PANCREATIC EDEMA
	Etiology
Chemical (*activated trypsin*); cause of activation thought to be the passage of *bile* under great pressure *into the pancreas* due to increased duct pressure; this is caused by obstruction at the sphincter of Oddi by stone or by spasm	*Bacterial. The infection may be systemic* (like mumps), or local, ascending from the duodenum; rarely, it is caused by emboli
	Pathology
Necrosis of pancreatic tissue due to digestion by activated trypsin, and chemical peritonitis and fat necrosis caused by release of steapsin	*Cloudy swelling of pancreatic cells, inflammation of connective tissue, and, in some cases, suppuration with abscess; if due to the streptococcus, may be necrosis and a resemblance to the hemorrhagic type; peritonitis rarely occurs; when it does, is bacterial in type*
	Symptoms and Signs
Sudden onset, intense pain, shock, little *fever, high leucocyte count, rigidity,* vomiting, high blood diastase, and, frequently, glycosuria: *usually occurs after a heavy meal, at which time bile is poured forth*	Slow onset, less pain, more fever, higher *leucocyte count, less rigidity, palpable* mass, vomiting, normal blood diastase, and, rarely, glycosuria
	Prognosis
Serious	Less serious
	Treatment
Fat free diet, fluids, relief of pain, and "peritonitis regimen" if diagnosis can be made; if in doubt, surgical exploration; recently partial pancreatectomy has been tried	Fat-free diet, fluids, and, if an abscess forms, drainage

In both types an increase in intraluminal pressure occurs. Rich believes that in some instances a metaplasia of the epithelium of the ducts causes obstruction. In the hemorrhagic type, atheroma of the pancreatic vessels is said to be a factor.

Associated pathological states include (1) liver edema and cloudy swelling of the cells around the central vein and portal areas with necrosis; this may account for the severe toxemia occurring in acute pancreatitis; (2) suppuration in the pancreas and rarely liver abscess as well; (3) gallstones or other biliary tract disease as a predecessor or common duct ob-

struction as a result of edema or fibrosis or both; (4) chemical peritonitis with fat necrosis with subsequent infection resulting in bacterial peritonitis; also "bile" peritonitis.

Variations in symptoms and signs are many. The predominating symptoms are pain, nausea, and vomiting. Since these symptoms are common to so many intra-abdominal and even thoracic and cardiac diseases, they mean very little alone. Shock is usually present but not always. If there is shock and rigidity in the upper abdomen and some cyanosis, the diagnosis is more apparent and tends to rule out perforated peptic ulcer where there is rarely shock and the rigidity is more general. Although the above picture does simulate acute coronary occlusion, mesenteric thrombosis must be thought of because in both conditions the pain, adynamic ileus, high leucocyte count, and all other symptoms and signs may be very similar.

In mesenteric thrombosis, blood is usually found in the stool; in pancreatitis, none is present as a rule. Rarely this does occur. Coronary occlusion may mimic pancreatitis. In both conditions there may be low blood pressure and pain in the epigastrium (in the case of pancreatitis, local tenderness and rigidity). If a friction rub is present over the precordium, the differential diagnosis is easily made.

The picture may resemble mechanical bowel obstruction, acute alcoholism, acute perforating appendicitis, renal colic, and twisted ovarian cyst.

The laboratory aids in the differential diagnosis are as follows: (1) Elevated blood amylase during the first forty-eight to seventy-two hours, The *urinary diastase* becomes elevated after twelve to twenty-four hours and remains elevated longer. Therefore, both tests should be done. If there is extreme destruction of the pancreas, the blood amylase may actually fall. (2) Depressed blood calcium due to utilization of ionizable calcium. Pancreatic lipase acts on fats, splitting them into glycerol and fatty acids. Calcium unites with free fatty acids, forming soap. Enough calcium may be used up to cause tetany. (3) X-ray which shows gaseous distention of overlying viscera (stomach and transverse colon). (4) Glycosuria and hyperglycemia which may occur due to destruction or inhibition of islands of Langerhans.

Treatment.—

If the diagnosis is established, then surgery should be withheld. The patient is treated conservatively. Water balance and blood volume are maintained by adequate parenteral fluids, plasma, and blood transfusions. Distention is controlled by the Levine tube with suction. Demerol is given in adequate amounts to control pain, nitroglycerine to relax the sphincter of Oddi, atropine to reduce gastric and pancreatic secretions. X-ray treatment may be of value according to some observers.

If the surgeon is not sure of the diagnosis, exploration is indicated. Should pancreatitis be found, closure is accomplished without drainage,

using silk sutures or other nonabsorbable material. Interference with the biliary tree is not desirable unless gallstones are present; if gallstones are present, their removal with cholecystostomy or choledochostomy may be indicated. If drainage is necessary for collections of fluid or pus in the lesser peritoneal cavity, drainage is accomplished through stab wounds in the right and left hypochondrium but not through the incision because of the dangers of digestion and wound dehiscence even though catgut closure is avoided. Psuedocysts may be drained or marsupialized. A few cases of resection of the necrotic portion of the pancreas have been reported with results that are fairly promising.

Should conservative management fail, surgery may be necessary to drain the lesser peritoneal sac or an abscess. These are cases of true pancreatic necrosis which are rare. In such cases right splanchnicectomy has been advocated.

Recurrent attacks of pancreatitis are usually of the parenchymatous type. They are best treated by a dietary regimen restricting the quantity of food at any one time, alcohol, and fatty foods. Surgical drainage of the common duct by T tube, cholecystectomy, and dilation and even cutting of the sphincter of Oddi have been suggested, but the results have been disappointing. Results have been more gratifying with conservative treatment. Complications such as pseudocysts, fibrosis, and calcifications are best treated by partial pancreatectomy. Left splanchnicectomy is said to be helpful even after complications occur.

Chronic interstitial or *parenchymatous pancreatitis, chronic relapsing pancreatitis,* is far more common than is generally believed. It may be produced by repeated attacks of acute parenchymatous or hemorrhagic pancreatitis or by a progressive lesion. Gallstone formation is a frequent complication but is not known to be causative. The changes in the pancreas vary, and indeed the acute phase of a recent attack with edema, inflammation, hemorrhagic necrosis, and abscess may be superimposed on the chronic changes of atrophy, fibrosis, cyst formation, calcification, and stone formation. In a recent case pancreatectomy was done, and the duct epithelium showed a piling up of the columnar lining cells with papillary infolding in addition to the changes mentioned.

The syndrome of chronic pancreatic insufficiency is characterized by steatorrhea, malnutrition, weakness, hypotension, hypoproteinemia, vitamins K and D deficiency. In the recurrent types of acute pancreatitis, diabetes ultimately occurs. Symptoms include chills, slight fever, diarrhea, nausea, vomiting, and some jaundice. Sometimes an epigastric mass with enlarged liver and spleen may be felt. Laboratory examinations may reveal anemia, hypoproteinemia, albuminuria elevated serum lipase and amylase at times, hyperglycemia, elevated serum bilirubin, and abnormal glucose tolerance curve. The disease may mimic the acute type and all of the lesions with which this type may be confused. In addition, carcinoma of the pancreas or of the ampulla of Vater may cause pancreatitis which at

first resembles primary chronic pancreatitis, but, of course, carcinoma is progressive. Nontropical sprue also resembles chronic pancreatitis.

Treatment may be medical, with careful dietary management as previously described. Surgery may be necessary for gall bladder disease, stones in the pancreas, cysts, or chronic painful pancreatitis. The cysts may be drained, or pancreaticolithotomy done, or partial pancreatectomy may be required especially to relieve persistent and disabling pain. Other surgical measures which have been advocated are subtotal gastrectomy (to reduce gastric acidity and therefore secretin formation); vagotomy (also reduces gastric acidity); splanchnicectomy (to increase blood supply and to inhibit reflex vasospasm to other organs, namely, lungs and gastrointestinal tract; also decrease pain).

Neoplasms and Cysts of the Pancreas

Benign neoplasms of the pancreas are not common. They include fibroma, chondroma, lipoma, myxoma, and adenoma.

Adenomas may be solid or cystic, and the latter may be of the proliferating papillary type. *Islet-cell adenomas* are of importance because they may be secretory, producing an excess amount of insulin, with resulting hypoglycemia. There may be only one tumor or many or a diffuse adenomatosis. They are usually located in the tail but may be anywhere on the gland, deeply within the gland, or extrapancreatic. They may be benign, histologically malignant but not metastasizing, malignant with metastasis. Lastly, they may be functionally active in the young or inactive in the older groups, and it is not possible to tell by examining the beta cells which are secretory and which are not. The tumors resemble normal pancreatic tissue, are round, and usually are well defined by compression (false capsule) or true capsule. Their microscopic appearance resembles an enlarged islet. The tumor is probably derived from the ductules but may be derived from pre-existing islets. The symptoms and signs may be extremely sparse or nonexistent except for the palpation of a mass. Usually, *however, the symptoms are those of hyperinsulinism and* hypoglycemia and exhibit Whipple's essential triad: attacks of central nervous system disorder—motor, vasomotor, psychic; coming on during the fasting state; fasting blood sugar levels of 50 mg. per cent or less and immediate recovery from attacks upon administration of glucose by mouth or vein. A tumor may or may not be felt before operation or during surgery. If the latter is true, a wide search should be made for extrapancreatic tissue and failing in this search, the lesion may be considered a hyperplasia or diffuse adenosis of the pancreatic islets. If the symptoms persist after subtotal resection, pancreatic islet adenomas may have been overlooked outside the pancreas. Differential diagnosis includes liver disease, affecting glycogen storage, and diseases of the adrenal cortex, anterior lobe of the pituitary, and the thyroid gland, producing hypofunction. A test which may aid in the diagnosis is the glucose tolerance, which

is normal except for the initial value (low) for about three hours and then drops sharply, and, unlike the normal, returns to average value due to the compensatory secretion of adrenaline; it stays down due to oversecretion of insulin. Epinephrine and pituitary extract do not raise the blood sugar as much as in the normal, and insulin lowers it more than normal.

The treatment is surgery with removal of the tumor or tumors or subtotal pancreatectomy and rarely total pancreatectomy.

Malignant neoplasms include primary carcinomas of the islet-cell type or acinus duct type, sarcomas of the spindle-cell variety; or lymphosarcoma, and, rarely, secondary carcinomas or sarcomas, especially the melanoblastomas.

Primary carcinomas are more frequently scirrhus than medullary; microscopically they may be of the adenocarcinoma, simplex, or mucinous types. The growth may extend into the duodenum or surrounding tissues or organs and may metastasize to the neighboring nodes or the liver. It may occur in the head or tail of the pancreas or may involve the entire gland. *Symptoms* and *signs* include rapid weight loss, boring upper abdominal pain with penetration to the back, jaundice, palpable nontender gall bladder (Courvoisier's law), gastric and intestinal disturbances including nausea, vomiting, partial obstruction. Laboratory findings which are helpful are alcholic stools, no urobilinogen in the urine, high serum lipase, normal serum amylase, excess of fat and nitrogen in stools. X-ray studies show deformities in adjoining hollow viscera. Carcinoma of the *tail* of the pancreas may give rise to severe persistent boring pain in the left upper quadrant and epigastrium which is referred to the back. This may be the *only symptom* or sign. There may be diabetes and sugar tolerance disturbances, ascites, widespread metastases, phlebothrombosis, and edema in the portal and systemic venous circulations especially in the mucinous carcinomas, splenomegaly, some deformities in the stomach or duodenum as seen by x-ray examination. The *association* of *weight loss* and *abdominal pain* in the epigastrium with negative physical and gastrointestinal x-ray findings should suggest the possibility of carcinoma of the pancreas. The differential diagnosis includes silent common duct stone, hepatic disease with jaundice, chronic pancreatitis with edema and obstruction of the common bile duct, pancreatic calculi, and carcinoma of the ampulla.

The treatment is surgical, requiring subtotal or total pancreatectomy if feasible. Contraindications to surgery include distant metastases, extensive local spread (although the spleen, a portion of the liver, the stomach, the duodenum, and transverse colon have been removed when involved), and involvement of the portal or the superior mesenteric vein. The steps of the operation (Whipple): (1) right paramedian or transverse incision; (2) search for metastases to liver and adjacent organs; (3) incision of peritoneum to the right of the duodenum and mobilization of duodenum to determine mobility of pancreas; (4) examination of pancreas to determine site of emergence of superior mesenteric vessels, the presence of an uncinate process, and the degree of encirclement of this process; (5)

separation of the common duct from the portal vein in the gastrohepatic omentum or hepatoduodenal ligament well below the cystic duct and behind the duodenum where it is divided between clamps; (6) the pyloric end of the stomach is freed and divided between clamps; (7) ligation of the gastroduodenal artery after it is identified so that the hepatic artery will not be accidently tied and cut; (8) division of the duodenum or jejunum, depending on the extent of the carcinoma and presence of an uncinate process; if the latter is present, it must be separated from the superior mesenteric vessels which lie anterior to it as well as posterior to the neck of the pancreas; (9) the inferior pancreatico-duodenal artery is tied and divided; (10) division of the pancreas anteriorly at the junction of the head and body, and dissection of the splenic vessels and portal vein and superior mesenteric vessels away from the head of the pancreas; the head of the pancreas, pyloric end of stomach, duodenum, and end of common duct are removed as a unit; the duodenum (or jejunum) is closed; (11) end-to-side gastrojejunostomy of a loop of jejunum or a vertical limb in which a Roux type of jejunojejunostomy has been done; (12) anastomosis of the pancreatic duct to the jejunum over a small rubber catheter proximal to the gastrojejunostomy; (13) end-to-side or end-to-end anastomosis of the common bile duct to the jejunum, depending on whether a loop or vertical limb of jejunum was employed. Sometimes a total pancreatectomy may be necessary; in such cases impairment of gastrointestinal function will result unless pancreatin is administered and the diet is high in calories, protein, and carbohydrate and low in fat. Should resection not be feasible, palliation may be obtained by (1) cholecystoduodenostomy or choledochoduodenostomy or chelecystostomy in desperate cases to relieve obstruction of the biliary tract; (2) gastrojejunostomy to relieve obstruction; (3) reduction in size of tumor by ligation of the major blood supply. Since biopsy of pancreatic lesions is often unreliable, a cholecystoduodenostomy may be done in doubtful cases. Later, a second operation may be done. If the pancreas has decreased in size, the lesion may be considered benign; if not, pancreatectomy is indicated.

Pancreatic cysts may be classified as follows:

1. Developmental cysts
   a. Congenital
   b. Fibrocystic disease of pancreas
   c. Inclusion cysts
2. Distention cysts
   a. Retention (lined by epithelium and due to obstruction)
   b. Exudation (due to degenerative changes, hemorrhagic cysts, pseudocysts)
   c. Extravasation (traumatic, pseudocysts)
3. Cysts of new formation
   a. Dermoid cysts
   b. Teratoma
   c. Cystadenoma
   d. Cystadenocarcinoma
   e. Parasitic cysts (hydatid)

is normal except for the initial value (low) for about three hours and then drops sharply, and, unlike the normal, returns to average value due to the compensatory secretion of adrenaline; it stays down due to oversecretion of insulin. Epinephrine and pituitary extract do not raise the blood sugar as much as in the normal, and insulin lowers it more than normal.

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3. Cysts of new formation
   a. Dermoid cysts
   b. Teratoma
   c. Cystadenoma
   d. Cystadenocarcinoma
   e. Parasitic cysts (hydatid)

The cysts may be present in the gastrohepatic omentum, the transverse mesocolon, or the gastrocolic ligament. The symptoms and signs vary with the size and location of the cyst. There are usually pain in the epigastrium referred to the back, pressure symptoms on neighboring organs which may produce nausea, postprandial discomfort, vomiting, and distention. Often the swelling may be felt as a smooth fixed mass. X-ray helps materially, revealing distortions or obstructions in hollow viscera. Since the cyst may fill a great portion of the abdomen, it may have to be distinguished from hydrops of the gall bladder, mesenteric cyst, hydronephrosis, cysts of the liver or the ovary.

Treatment consists of removal of the cyst or subtotal pancreatic resection if at all possible. If this cannot be done, the cyst may be drained externally by marsupialization or internally by anastomosis to the stomach, duodenum, or jejunum.

Fibrocystic disease of the pancreas is frequently associated with respiratory disease (bronchiectasis) and a great nutritional disturbance. Recently right total splanchnicectomy has been advocated for its treatment.

The Spleen

The spleen normally weighs about 160 grams and measures 12 by 7 by 4 cm. It is of mesodermal origin and originates as a thickening of the dorsomesogastrium due to division of cells of the peritoneal mesogastrium and also of the mesenchymal cells. The spleen develops in the cranial portion of the greater omentum, and that portion of the greater omentum which extends between the stomach and the spleen is known as the gastrolienic ligament. The dorsal wall of the omentum between the spleen and the kidney is known as the lienorenal ligament. The first vascularization is by a capillary network which forms into the intrasplenic arteries and veins. The undifferentiated capillaries between them form the capillary tufts or spherules. These become transformed into pulp. The spleen is supplied with blood by the splenic artery which is a branch of the celiac axis and which lies behind the stomach, giving off small (vasa brevia) branches to the fundus of the stomach. The artery, as has been said, breaks up into many branches as it enters the hilus in the lienorenal ligament. The splenic vein runs along with the artery and pours its blood into the portal system. The spleen is held in place by the lienorenal ligament which carries the blood supply, the gastrosplenic ligament, which is continued as the gastrocolic ligament, and the phrenocolic ligament which forms somewhat of a sling for the spleen to rest upon. The spleen lies in close contact with the stomach, the diaphragm (which many times has numerous small arterial twigs in its adhesions to the spleen), the pancreas, the anterior surface of the left kidney, the splenic flexure of the colon.

The spleen is covered by thin elastic capsule which adheres to the underlying tissue. It is thickened at the hilus where the arteries and veins enter and leave the viscus. The trabeculae are continuations of the capsule which penetrate the organ and form its framework. Splenic tissue resembles lymphatic tissue, and this fills the space between the trabeculae and consists of red pulp and white pulp. The white pulp is often called malpighian bodies. They consist of diffuse and nodular lymphatic tissue which surround the terminal subdivisions of the splenic artery. The red pulp is dark red in color and can be scraped from the cut surface. The veins seem to be connected with the red pulp, whereas the arteries seem to be connected with the white. The connections between the veins and the arteries have given rise to much speculation and the three main theories are as follows:

1. That the arterial capillaries open directly into the pulp spaces between the reticular cells of the splenic cords and the blood gradually filters into the venous sinuses

(the open circulation theory), irregular, inconstant channels, lined by fixed and wandering cells and reticulum. They are a plexiform three dimensional system of channels which intercommunicate. They are 6 microns wide and may enlarge in Banti's disease to 16 microns.

2. That the arterial capillaries communicate directly with the lumen of the venous sinuses (the closed circulation theory).

3. That both types of circulation are present. The collagenous fibers of the trabeculae are continuous with the reticular fibers in the white pulp. In the center of the lymphatic nodules, just as in the nodules of lymph nodes, the framework consists of thin scattered threads, and lymphocytopoietic centers are present in these areas. In the red pulp venous blood vessels are called venous sinuses and appear as cords. These have been known as the splenic or Billroth cords. They run in all directions from a spongy framework throughout the venous sinuses. The venous sinuses do not contain vascular endothelium but are lined by long narrow cells arranged parallel to the axis of the vessels. These lining cells are macrophages, identical in origin and properties with those of the adjacent splenic cords and their cells. The spleen may be looked upon as a vast reticulo endothelial sponge with a supporting framework of trabeculae and reticulum and a certain amount of lymphoid tissue. There are no lymphatics in the splenic pulp. There are some in its capsule.

When the spleen is removed in man, (1) anemia develops to about 3,000,000 red blood cells, but this returns to normal in about two months; (2) a leucocytosis occurs, mostly polymorphonuclears—20,000 to 30,000, also thrombocytosis; (3) the spleen makes erythrocytes thicker and more fragile to hypotonic solutions; the fragility of red blood cells is decreased; Howell Jolly bodies in the erythrocytes and target cells (abnormally thin erythrocytes) are found; these are less fragile; (4) hemolytic substances produce jaundice less readily; (5) in pernicious anemia the urobilin in the urine is decreased, showing less red blood cell destruction; there is also a lowered urobilinogen output in the feces after splenectomy.

In experimental animals such as rats there is a definite decrease in the resistance to infection and a hypertrophy of the reticulo endothelial cells of the body.

Hyperactivity of the spleen seems to sensitize the red blood cells for easy destruction by the liver. It is thought that splenectomy is beneficial in many diseases accompanied by splenomegaly, not because of removal of injurious substances produced by the spleen, or normal inhibitory mechanisms such as normal serum lysin, but chiefly because it relieves the liver of a vast amount of work since 25 per cent of the portal blood going through the liver is from the spleen normally. Perhaps this explains the amelioration of symptoms such as jaundice, toxic symptoms, and leg ulcers. The leg ulcers are relieved due to collateral circulation around the portal system, less venous stagnation in the local extremities, and less stagnant anoxia.

The physiology of the spleen seems to be as follows:

1. The destruction of red blood cells—not normal ones but those which are worn out, damaged, or abnormal.

2. Storage of blood and the emptying of this storage during hemorrhage due to the contraction of muscle fibers in the capsule and trabeculae. The contraction results from stimulation of the sympathetic nervous system. Normally one-fourth of the total erythrocytes and one-sixth of the total blood volume are stored in the spleen.

3. Manufacture of lymphocytes.

4. Reticulo-endothelial function which plays a role in immunity and removal of disintegrated red blood and other cells. In connection with this function, the role played in lipoid metabolism is extremely important.

5. A blood forming organ in the embryo.

6. Iron metabolism. There is a storage of pigment in the reticular cells and this is again utilized in the formation of hemoglobin. Splenic regeneration occurs from accessory spleens in a few cases.

7. The production of a hormone or hormones that seem to inhibit or control the output of cells by the bone marrow. In hypersplenism these hormones may be excessive,

greatly inhibiting blood cell production, or the spleen may destroy more cells than it should, *or both. In other words, the spleen* has a direct effect on the erythrocytes, leucocytes, and thrombocytes which traverse its sinusoids and indirect effects on the hemopoietic cells of the bone marrow.

The normal pressure in the portal vein is 8 to 12 mm. Hg or 108 to 162 mm. H_2O and slightly less in the coronary *vein and splenic vein. In the inferior vena cava it is* about 4 to 5 mm. Hg or 40 to 110 mm. H_2O, depending on the position of the arm. In portal hypertension the portal pressures become very high.

Congenital Anomalies of the Spleen

The spleen may be entirely absent or may be on the right side in cases of *situs inversus. There may be a double spleen with an independent* vascular pedicle derived from the splenic artery and vein. Fissures and lobulation occur infrequently. *Accessory spleens* are common in children and decrease with advancing age, although we have recently operated upon a woman 32 years of age with Banti's disease with a double spleen and twelve accessory spleens. Accessory spleens probably disappear as age advances unless the individual has some intrinsic pathology such as congenital hemolytic icterus. The position of the accessory spleens is variable but generally they are in the hilar region or the splenic pedicle, less often surrounding the tail of the pancreas, the greater omentum close to the greater curvature of the stomach, the splenocolic ligament, the mesentery of the small and large bowel, the left broad ligament, the ovary, the tunica vaginalis, and retroperitoneal space. *Splenosis* is probably *an acquired lesion* in which multiple splenules may be found throughout the abdomen and may run into the hundreds. These spleens *are thought to be autotransplants resulting from* traumatic rupture, spontaneous rupture, and even accidental rupture during splenectomy. *Accessory spleens are unimportant except in diseases* where splenectomy is indicated. If in such cases accessory spleens are overlooked, the symptoms *may not be ameliorated. Occasionally the spleen* has a long pedicle and moves freely through a wide area. It may become twisted on its *pedicle.*

Injuries of the Spleen

The spleen is commonly ruptured by a fall or blow on the abdomen without any external wound. Penetrating wounds may also cause a tear in the spleen. Sometimes there is a splenic tear without apparent cause or following a coughing spell or sneezing or straining, due probably to adhesions pulling on a movable spleen or pressure by adjacent viscera when the abdominal muscles contract when the spleen is fixed. "Spontaneous" rupture also occurs without any apparent cause, and the spleen may be normal. More often, the spleen is the seat of some pathological process, primarily or secondarily, such as malaria, infectious mononucleosis, leucemia, typhoid, Banti's syndrome, tropical splenomegaly, etc. In malaria there is reticular and endothelial hyperplasia which obstructs the venules and sinuses, causing interstitial and subcapsular

hemorrhages that may lead to rupture. Indeed traumatic rupture may be produced in such a way that the capsule is not torn; blood accumulates under the capsule, causing a tear with massive hemorrhage days or even weeks after the injury. This is called "delayed rupture" of the spleen.

The symptoms and signs will be mild in the absence of hemorrhage—Left upper quadrant pain which radiates to the left shoulder, especially when a deep breath is taken, left-sided muscle spasm, and tenderness on palpation. Sometimes a mass may be felt. With great blood loss there is shock. Laboratory aids include a leucocytosis, which in our experience appears early and before there is a decrease in the red blood count; and x-ray studies, which show some distortion of adjacent viscera, especially the stomach, which contains gas, soft tissue mass, and elevation of the diaphragm, with evidence of free fluid between intestinal loops.

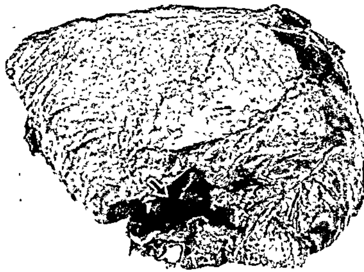

Fig. 379.—Traumatic rupture of the spleen. The patient, a man aged 60 years, was in an automobile accident. Arrow points to the tear.

Treatment consists of adequate preparation by blood replacement and immediate splenectomy to prevent fatal hemorrhage.

"Wandering spleen" is the term used to describe a spleen with an abnormally loose attachment and pedicle which moves to various positions in the abdomen, usually without symptoms or danger and commonly seen in multiparous women. Treatment will usually consist of exploration because of the difficulty in making the diagnosis of the palpable movable mass and its variable symptoms. Should the spleen become twisted on its pedicle, it would become swollen due to the trapping of venous blood until the pressure in the veins and their tributaries equalled the arterial pressures, causing anoxia and infarction. The

patient would complain of severe pain, and the mass would be palpable and tender. Splenectomy should be done in case of torsion and is probably indicated when torsion is not present because anchorage of the spleen is not satisfactory. The abnormality is rare. We have seen two cases.

Diseases and Infections of the Spleen

Splenomegaly or **splenomegalia** refers to enlargement of the spleen which may be due to many causes, some of which are but vaguely understood.

Group I Infections

- A. Nonspecific
  - 1. Primary abscess following trauma or infarction or hematoma or thrombosis of splenic vein
  - 2. Secondary abscess from pyemia, typhoid fever, puerperal sepsis, embolism, extension of adjacent suppurative processes
- B. Specific
  - 1. Primary
    - a. Tuberculosis
  - 2. Secondary involvement or enlargement due to the spleen's action as a filter or phagocytic organ
    - a. Tuberculosis
    - b. Malaria
    - c. Syphilis
    - d. Kala azar
    - e. Chronic sepsis
    - f. Schistosomiasis
    - g. Histoplasmosis (may also cause hepatomegaly)
- C. Amyloidosis of spleen secondary to chronic infections anywhere in the body (tuberculosis, chronic empyema, etc.)
  - 1. Primary amyloidasis in which the cause is unknown

Group II. Lipoid dyscrasias

- A. Generalized forms
  - 1. Lipoidosis or xanthomatosis
  - 2. Primary or essential xanthoses
    - a. Gaucher's disease
    - b. Niemann Pick's disease
    - c. Hand-Schüller-Christian's disease
    - d. Primary nonsymptomatic external and internal xanthomatoses
  - 3. Lipoid neoplasms
    - a. Lipoma
    - b. Xanthomatous carcinoma
    - c. Xanthomatous sarcoma

Group III. Lymphatic dyscrasias, lymphoblastic diseases

- A. Lymphatic leucemia
- B. Splenomyelogenous leucemia
- C. Hodgkin's disease
- D. Agnogenic myeloid metaplasia
- E. Lymphosarcoma of the spleen

Group IV. Anemias with primary or secondary disease of the liver or hepatomegaly

- A. Banti's syndrome (Banti's disease, congestive splenomegaly, splenic anemia)
- B. Cirrhosis of the liver
- C. Erythroblastic anemia (Cooley, von Jaksch)
  1. Thalassemia major and minor
- D. Hemochromatosis
- E. Diseases in this group associated with arthritis
  1. Still's disease (rheumatoid arthritis of children)
  2. Felty's syndrome (in adults)

Group V. Erythremia

- A. Polycythemia vera, splenomegalic polycythemia, Vaquez's disease, Osler's disease
- B. Symptomatic or secondary polycythemia may be accompanied by splenomegaly
  1. Tetralogy of Fallot
  2. Pulmonary stenosis
  3. Pulmonary arteriosclerosis (Ayerza's disease)
  4. Congenital polycythemia
  5. Polycythemia with hypertension in elderly patients

Group VI. Hemolytic, leucocytolytic, and thrombocytolytic diseases

- A. Hemolytic
  1. Hemolytic (spherocytic, acholuric) jaundice
  2. Acute hemolytic anemia (Lederer)
  3. Sickle-cell anemia
- B. Leucocytolytic
  1. Splenic neutropenia
- C. Thrombocytolytic
  1. Thrombocytopenic purpure (Werlhof's disease, idiopathic thrombopenic, purpura hemorrhagica)
- D. Combined form
  1. Splenic panhematocytopenia

Group VII. Neoplasms and cysts

- A. Neoplasms
  1. Primary
     - a. Benign—Fiboma, lymphoma, hemangioma, lymphangioma, chondroma, osteoma, leiomyoma
     - b. Malignant—Fibrosarcoma, leiomyosarcoma, endothelioma, hemangioendothelioma, angiosarcoma, lymphosarcoma, reticulum-cell sarcoma
  2. Secondary malignant neoplasms (by blood stream, which is very rare, by contiguity, or by generalized abdominal seeding); metastases from any organ but stomach carcinoma most common
- B. Cysts
  1. Distention cysts
     - a. Retention—dilatation cysts, polycystic disease due to ectasia of splenic sinuses
     - b. Infoliation cysts due to peritoneal inclusions

2. Cysts of new formation
   a. Traumatic arising from hematoma
   b. Degenerative cysts *following infections or infarctions*
   c. Neoplastic
      (1) *Dermoid*
      (2) Epidermoid
      (3) *Hemangiomatous*
      (4) Lymphangiomatous
      (5) Cystic degeneration in neoplasms
   d. Parasitic
      (1) Hydatid disease

Group VIII. Vascular splenic enlargements

A. Aneurysm of splenic artery
B. Arteriovenous fistula due to wounds
C. Embolism in subacute bacterial endocarditis and auricular fibrillation
D. Thrombosis of the splenic vein from inflammation, trauma, pressure from without by inflammatory disease or neoplasms, polycythemia vera

Group I. Infections.—*Nonspecific* infections with abscess formation due to primary or secondary causes are more common than is ordinarily supposed. The abscess, as in the liver, is apt to form large necrotic masses. The symptoms and signs are those of an acute septic focus with chills, fever, high leucocyte counts. After the splenic capsule becomes involved, there is pain, rigidity, and tenderness over the spleen. The pain radiates to the left shoulder and is intensified on deep breathing. A left subphrenic abscess gives almost the same symptoms and may occur as a complication. Also, the left pleura may be involved, giving rise to effusion or empyema. *Splenectomy is indicated* because of the extensive tissue destruction, the possibility of multiple necrotic areas, and the possibility of sloughs with hemorrhage after simple drainage which some surgeons regard as the treatment of choice.

Of the *specific infections*, only "*primary*" *tuberculosis* of the spleen warrants splenectomy. Even here it is doubtful whether the disease is primary in the spleen.

Group II. Lipoid Dyscrasias.—The spleen acts as a filter in disturbances of lipoid metabolism. There are three generalized forms:

1. Xanthomatosis or lipoidosis. It may be symptomatic, as in diabetes or in jaundice. These dyscrasias are due to a cholesterolemia and selective absorption of the cholesterol fatty acids by the xanthomatous cells. There are deposits in the skin and lymph vessels over the body. These vary in size from a pea or bean and are yellow or brownish and appear as nodules in the skin. The spleen may be enlarged, and the large phagocytes appear as foam cells. They are entirely from the reticulum cells of the pulp. The endothelial cells are not affected.

2. Primary or essential xanthoses. In this group may be placed Gaucher's disease, Niemann-Pick's disease (greatly enlarged spleen and

liver and discolored skin), Hand-Schüller-Christian's disease, and primary nonsymptomatic external and internal xanthomatoses.

3. True neoplasms which may be accompanied by enlarged spleen, such as xanthomatous carcinoma or sarcoma and xanthoma en tumeurs of the skin occurring around the knee, elbow, and heel.

Weber-Christian's disease is a febrile relapsing nonsuppurative panniculitis and is thought to be a lipoid histiocytosis. Bazin's erythema induratum and Darier's sarcoid are said to be related to fat necrosis and lipophage granulomas.

Of this group, splenectomy is indicated in Gaucher's disease, where it may be used as a palliative measure, and in the true lipoid neoplasms of the spleen which cannot be diagnosed preoperatively. Gaucher's disease is a chronic lipoid disturbance producing a splenomegaly. There is a familial tendency, and sometimes it is congenital. The reticuloendothelial cells contain an excessive storage of kerasin (a cerebrosid) giving rise to the Gaucher's cells which appear in the spleen, liver, lymph nodes, and bone marrow. Clinically, Gaucher's disease occurs mostly in girls under the age of 5 years but may occur also between the ages of 25 and 35 years. It is a chronic and progressive disease with brownish-yellow discoloration of the skin of the face, neck, and hands and pingueculae of the conjunctiva. The splenomegaly is progressive but without ascites. There is apt to be generalized lymphadenopathy and hepatomegaly. Hemorrhages occur, and there may be convulsions Laboratory tests will show a hypochromic anemia, leucopenia, and thrombocytopenia. Biopsy of the spleen, lymph nodes, and bone marrow shows the Gaucher's cells which appear in no other disease. They are large with small eccentric and sometimes multiple nuclei and do not stain with fat stains and are not doubly refractile. X-ray examination of bones shows a nodular appearance with osteoporosis but no cortical infiltration. Death is usually due to an intercurrent infection. Tuberculosis is common. Splenectomy is indicated because of the great destruction of blood cells and platelets, the hemorrhagic tendency, and the increasing size of the spleen, but it must be regarded as palliative.

Group III. Lymphatic Dyscrasias.—These have been discussed in Chapter 17. *Splenectomy is not indicated* in such diseases and may actually be harmful. This is especially true in agnogenic myeloid metaplasia of the spleen, a disease of unknown etiology associated with fibrous unproductive bone marrow in which the spleen takes on its embryonic function of producing red blood cells. The syndrome is observed from infancy to old age and is characterized by splenomegaly and the presence of immature red and white cells in the blood. It may be confused with chronic myelogenous leucemia, splenic anemia, erythroblastosis, or Hodgkin's disease. Careful studies of the blood and bone marrow cells and fragility tests will help to identify the condition. This is important because splenectomy or radiation therapy of the spleen takes away the only source of hematopoiesis.

Group IV. Anemias With Primary or Secondary Disease of the Liver or With Hepatomegaly.—

Banti's syndrome (Banti's disease, congestive splenomegaly, splenic anemia) was originally described by Banti as a disease in which there were three stages: anemic, with gastrointestinal hemorrhage and

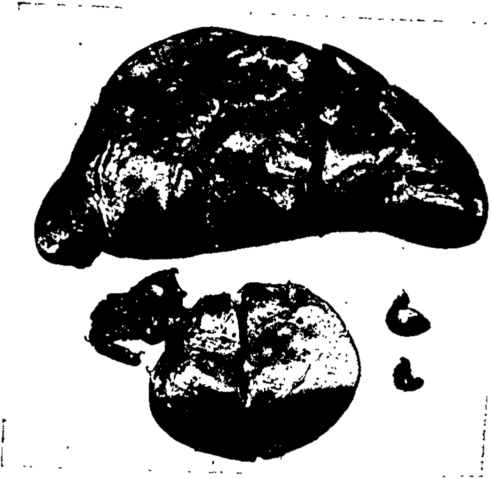

Fig. 380.—Banti's syndrome with multiple spleens. M. H. was a white woman 34 years of age who came to the hospital complaining of soreness in the right upper quadrant of the abdomen for a period of five years. The past history showed that there was a swelling in the right upper quadrant for the past two years and that it was increasing in size. On examination it was found that there was a tumor mass extending down from the costal margin for a distance of about 8 cm., and it extended across the midline into the left upper quadrant. The patient was diagnosed as having an enlarged liver and spleen. There was no jaundice, no hematemesis, and no ascites.

She was operated upon in March, 1948. At this time there was no ascites and the liver was not greatly enlarged, but it was nodular and hard. The venous pressure in the antecubital vein was 100 mm of water; in the portal vein, 290 mm. of water; and in the splenic vein, 260 mm. of water. The normal pressure in the antecubital vein is anywhere from 40 to 110 mm. of water; in the portal vein it is about 8 to 12 mm. of mercury or 108 to 162 mm. of water. Therefore, the pressure within the portal vein in this case was almost double that of the normal. Because of the absence of ascites and esophageal varices and due to the numerous branches of the splenic vein, a splenorenal shunt was not attempted. Instead, the many spleens were removed. There was a very large spleen and a moderately large accessory spleen, the first measuring 21 by 9 by 6 cm. and weighing 750 grams. The large accessory spleen measured 10 by 7 by 4 cm. and weighed 750 grams. There were also sixteen other accessory spleens. These were proved to be so by histological examination. The pathological diagnosis was portal cirrhosis and congestive splenomegaly consistent with Banti's syndrome. The patient was last seen on June 1, 1949. At this time there was still no ascites. Patient has remained in good health. She has been on a high caloric diet with choline dihydrogen citrate, 1.5 Gm. four times a day. The photograph is that of the large spleen and the second largest accessory spleen together with three smaller spleens. Many of the smaller spleens were lost in the pathology laboratory so that they could not be photographed.

anemia; transitional, with oliguria, hepatomegaly, and brown disco tion; and ascitic, with atrophy of the liver, slight jaundice, ascites, hemorrhages. The syndrome included a "fibroadenic" thicke around the central arteries of the Malpighian corpuscles. Ba *syndrome has now come to imply* splenomegaly with anemia, leucop and thrombocytopenia, associated *with increased collateral cir* tion between the portal and systemic venous systems, and character *splenic changes (large* rough surface, perisplenitis, thick capsule, s sparse follicles, sclerotic portal and splenic *vessels, and dilated sinuso* Congestive splenomegaly may be caused by cavernomatous transfo*tion of the portal vein*, sclerosis, thrombosis, stenosis of the port splenic vein, or both. It is a mechanical *obstruction to the* p return and is frequently associated with atrophic cirrhosis of liver *which we have discussed* previously in this chapter. Rarely, plastic disease invades the portal vein.

The causes of obstruction, portal hypertension, and splenomegaly be *grouped as follows*:

A. Intrahepatic due to various *types of cirrhosis* of the liver (atro biliary) and chronic infections which ultimately result in cirr (*schistosomiasis*, infectious hepatitis)
B. Extrahepatic due *to various varieties* of portal occlusion
   1. Within the vein—thrombosis (inflammatory or traumatic)
   2. In the wall of the vein—stenosis (congenital or acquir phlebosclerosis)
   3. Compression on the outside by
      a. *Inflammatory* scar (following pancreatitis, cholangitis,
      b. Pancreatic cyst
      c. Pancreatic tumor
      d. *Aneurysm* of splenic artery
   4. Cavernomatous transformation of the *portal vein*

The *symptoms and signs* vary but usually the first evidenc splen*omegaly and* anemia. Hemorrhages are usually late, but somet the physician is first consulted because of *hematemesis* or bleeding the bowel. Later the enlarged liver shrinks, and there is ascites. Lab tory findings include, first, a normocytic and, later, with hemorrhag microcytic hypochromic anemia. There is practically always a leucop and thombocytopenia. The latter, together with hypoprothrombinemia dilation and thinning of the portal branches due to the hypertension, is cause of the bleeding tendency. In addition, the liver tests as previousl scribed *under* cirrhosis are helpful. The treatment depends entirely on the cause. If due to thrombosis *of the splenic* vein, splenect should be helpful by cutting down the volume of blood returning to liver. If in *the portal or if the* coronary vein joins the splenic an lously, then splenectomy would not help *greatly in reducing* the pr bility of esophageal varix bleeding. In fact, it may increase it due to

formation of more collaterals. In all types of portal obstruction, ligation and division of the splenic artery may materially reduce the volume of blood returning from the spleen but is not entirely without danger of necrosis, although we have not encountered this complication. Sometimes the spleen is not greatly enlarged because of splenic infarction, destruction or adequate collateral circulation, or the short duration of the disease. Also, in elderly people with arteriosclerosis the splenic artery may become narrowed, cutting down the size of the spleen. In all of these instances splenectomy may be helpful but will probably do little more than give temporary symptomatic improvement. Therefore, the surgeon must be prepared to do a splenorenal shunt. Many methods have been devised to increase collateral circulation. These have been described previously under the heading of Portal Hypertension. They include omentopexy, portacaval shunt, splenorenal shunt and anastomosis between the superior mesenteric vein and the vena cava or other vessels of the two systems. Esophageal varices may be treated directly by resection of the lower esophagus and cardiac end of the stomach because ligations and injections of sclerosing agents have proved to be ineffective. At best the treatment of Banti's syndrome is to be regarded as symptomatic unless the cause is a mechanical block outside the liver.

Cirrhosis of the liver has been previously described in this chapter. The problem as related to the spleen is as in Banti's syndrome. Summary of treatment: Splenectomy is usually indicated because: (1) The spleen probably exercises an inhibitory effect on blood formation. (2) After splenectomy there is a rise in leucocytes and thrombocytes, although the erythrocyte rise is slower. (3) The enlarged spleen holds much blood and probably carries 30 to 40 per cent of the total portal flow. Its removal minimizes the enormous increase of blood volume which the esophageal varices may be forced to carry when the spleen contracts. To offset this hazard there is usually a prodigious amount of collateral blood flow into the systemic circulation through adventitious blood vessels in the adhesions between the spleen and surrounding tissues, especially the diaphragm.

If the block is in the splenic vein, splenectomy is curative. When the block is at any point closer to the liver than the entry of the inferior mesenteric vein, splenectomy alone will not suffice to cure bleeding from varices. A shunt must be done and this is best accomplished at the time of splenectomy.

There are two main types of shunts: (1) Splenorenal with preservation of the kidney used in most cases of extrahepatic block because most of the lesions are in the portal vein, precluding its use, and if not in the portal vein, extrahepatic splenectomy alone is curative. (2) Portacaval shunts are useful in intrahepatic types of block and are sometimes employed in cases that have had splenectomy at some previous time, leaving a scarred splenic vein not suitable for anastomosis. In the latter instances other veins may be used, particularly if there is cavernomatous

transformation of the portal vein; namely, superior mesenteric to vena cava, proximal end to side; inferior mesenteric to renal, proximal end to side; inferior mesenteric to vena cava, proximal end to side; inferior mesenteric to ovarian. (See Cirrhosis of Liver, this chapter.)

Erythroblastic anemia (Cooley, von Jaksch; thalassemia major if both parents have it and minor if one parent has it) is a disease of children which is hereditary and seen chiefly in Mediterranean races. The disease is one of abnormal blood formation and is apt to be fatal. The clinical features include splenomegaly and hepatomegaly which cause the abdomen to enlarge and generalized lymphadenopathy enlargement of the molar and cranial bones with skeletal bone changes (osteoporosis,

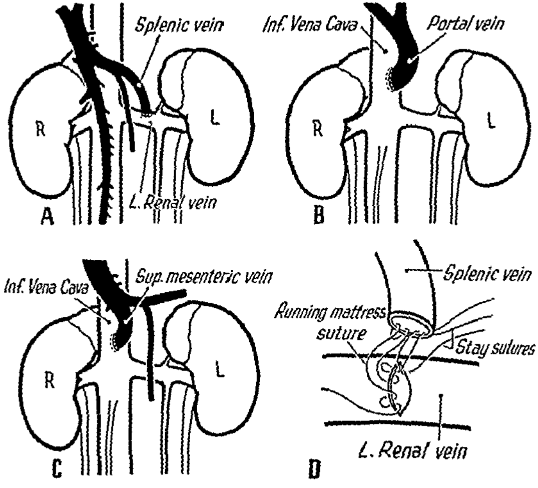

Fig. 331.—Diagram illustrating methods of shunting blood from the portal to the systemic venous system in portal hypertension. *A*, Splenorenal. Proximal end of the splenic vein to the side of the left renal vein. *B*, Portacaval. Anastomosis between the portal vein and the vena cava inferior. Exposure is obtained by a combined thoracoabdominal approach on the left, and for the portacaval anastomosis a thoracoabdominal incision is made on the right extending up into the eighth innerspace. *C*, Superior mesenteric-caval. Anastomosis here is between the proximal end of the superior mesenteric vein and the vena cava. *D*. The method of suture in splenorenal shunts. Other methods of diverting the portal blood into the systemic circulation have been used. These are described in Chapter 20 under the subject of ascites and in this chapter under the subject of portal hypertension.

formation of more collaterals. In all types of portal obstruction, ligation and division of the splenic artery may materially reduce the volume of blood returning from the spleen but is not entirely without danger of necrosis, although we have not encountered this complication. Sometimes the spleen is not greatly enlarged because of splenic infarction, destruction or adequate collateral circulation, or the short duration of the disease. Also, in elderly people with arteriosclerosis the splenic artery may become narrowed, cutting down the size of the spleen. In all of these instances splenectomy may be helpful but will probably do little more than give temporary symptomatic improvement. Therefore, the surgeon must be prepared to do a splenorenal shunt. Many methods have been devised to increase collateral circulation. These have been described previously under the heading of Portal Hypertension. They include omentopexy, portacaval shunt, splenorenal shunt and anastomosis between the superior mesenteric vein and the vena cava or other vessels of the two systems. Esophageal varices may be treated directly by resection of the lower esophagus and cardiac end of the stomach because ligations and injections of sclerosing agents have proved to be ineffective. At best the treatment of Banti's syndrome is to be regarded as symptomatic unless the cause is a mechanical block outside the liver.

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or hormones which greatly inhibit the production of blood cells by the bone marrow, or both mechanisms may be overacting at the same time. In any event there is splenomegaly and deficiency in the number of circulating erythrocytes, leucocytes, thrombocytes, or all of the elements. In addition to the many symptoms and signs that are common to the group as a result of the decrease in circulating blood cells, leg ulcers are present. These are difficult to explain and have been variously ascribed to decreased local resistance from peripheral vasoconstriction, stagnant anoxemia due to pressure on the venous system by the enlarged spleen, lymphedema, anemic anoxemia due to red cell destruction. The remarkable observation is that these ulcers promptly disappear after splenectomy.

HEMOLYTIC.—

1. Hemolytic (spherocytic, acholuric) jaundice is also known as hemolytic splenomegaly and congenital or familial hemolytic jaundice. Some observers distinguish between a congenital and an idiopathic acquired type. The latter is probably a subclinical congenital type manifesting itself in adult life. The cause is unknown. There is a diminution in size and number of the lymphoid follicles in the spleen, an engorgement of the pulp, and dilatation of the sinuses. Symptoms, signs, and laboratory findings include nonobstructive jaundice with a greatly enlarged spleen which is smooth, usually nonadherent, and greatly enlarged, weighing up to 1,500 grams or more. Both sexes are affected and complain of weakness, abdominal pain, vomiting, shortness of breath, and palpitation. Laboratory studies show an anemia, the presence of spherocytes (ballooned erythrocytes), increased fragility of red cells to hypotonic saline (normal erythrocytes begin to hemolyze in saline solution of about 0.45 per cent and are completely laked at 0.35 to 0.3 per cent; in hemolytic jaundice hemolysis begins at 0.7 per cent and is complete at 0.5 to 0.45 per cent), and reticulation of red blood cells. There is a positive indirect van den Bergh and urobilinogen in the urine. The disease goes through remissions and exacerbations (crises), and the latter may be severe enough to cause death. Two complications are seen: (1) Gallstones which are usually bile pigment soft stones due to the excessive amount of pigment in the bile and (2) leg ulcers. The treatment consists of small transfusions of plasma and blood followed by splenectomy which is curative, although the spherocytes remain. Much debate has arisen concerning surgery during a crisis. Most surgeons do not remove the spleen at this time and also do not advise transfusion at this time because the addition of blood with the great numbers of abnormal or devitalized cells usually introduced simply adds to the work of the already overactive spleen and may actually intensify the crisis. In addition, the presence of agglutinin-agglutinogen reactions is common, and theoretically at least the blood serum may contain destructive agents as is demonstrated by increased fragility which is simply the first step in red cell destruction. In other words, there may be an overproduction of hemolysins (auto- and iso-) and an underproduction of antihemolysins.

cortical atrophy, and thickening of medullary trabeculae). The bone marrow is hyperplastic. The laboratory studies show significant blood changes: erythroblastosis, anemia, achromia, anisocytosis and poikilocytosis, and leucocytosis. There is abnormal hemolysis which causes an increase in urobilinogen. The liver and spleen take on their primitive function of hematopoiesis to some extent. After splenectomy, normoblasts are greatly increased in the blood but soon disappear. Splenectomy is indicated and may retard the progress of the disease in addition to giving symptomatic relief because the spleen reaches an enormous size. However, it is not curative.

Hemochromatosis (bronze diabetes) is a metabolic disorder of unknown origin characterized by deposition of pigments, especially hemosiderin, in many organs of the body, cirrhosis of the liver and pancreas, diabetes, and splenomegaly. The spleen is fibrotic. The treatment is that of diabetes mellitus. Splenectomy is not indicated.

Splenomegaly with *arthritis* is seen in Felty's syndrome in adults and in Still's disease (rheumatoid arthritis) in children. *Felty's* syndrome consists of atrophic arthritis, splenomegaly, leucopenia, and normochromic anemia and hepatomegaly. It is attended by fever, loss of weight and strength, and brown pigmentation of the skin. A similar picture, seen in children with atrophic arthritis, is known as Still's disease. Whether the diseases are distinct entities or simply exaggerated manifestations of the arthritides of the rheumatoid type is open to question. Splenectomy is not curative but may give symptomatic relief, especially in Felty's syndrome.

Group V. Erythremia.—

1. *Primary erythremia* or *polycythemia vera* (splenomegalic polycythemia, Vaquez's disease, Osler's disease) is a disease of unknown origin occurring chiefly in male adults. The red blood count reaches from 9 to 10 million, and due to the enormous amount of circulating reduced hemoglobin, there is cyanosis. Splenectomy is not indicated unless there is splenic vein thrombosis with infarction which is extensive.

2. Secondary erythremia or polycythemia is seen as a compensatory mechanism so that oxygenation can take place in the presence of anoxic conditions due to the tetralogy of Fallot, pulmonary stenosis, pulmonary arteriosclerosis (Ayerza's disease), congenital polycythemia, and polycythemia with hypertension in elderly patients. Splenectomy is not indicated. Instead, measures are directed toward improved oxygenation of the blood.

Group VI. Hemolytic, Leucolytic, and Thrombocytolytic Diseases.— These constitute an ill-defined group of maladies which have in common an excessive destruction of blood constituents. This may be due to the overactivity of the spleen as a scavenger of abnormal cells, since in most instances there is a production by the bone marrow of immature or abnormal cells, or the spleen may be guilty of overproduction of a hormone

row or megakaryocytes or destroys the circulating thrombocytes. The latter concepts have not been proved clinically or experimentally, and the spleen is not enlarged because platelets are easily destroyed, nor does it show striking changes except enlarged germinal centers and the presence of megakaryocytes in the splenic pulp. Other theories seeking to explain the disease are faulty maturation of megakaryocytes so that they are easily destroyed and damaged or abnormal capillary endothelium. Symptoms and signs in the chronic variety are remissions and exacerbations which end in death from hemorrhage, or intercurrent infection, or spontaneous recovery, purpuric spots under the skin, fever, hemorrhages from any or all mucous membranes or from wounds or slight bruises. The acute form is more severe and is more apt to be fatal. Tests and laboratory studies help identify the disease. Evidence of increased capillary weakness and permeability is seen in the tourniquet test. If the venous return is occluded, petechial spots appear *promptly distal* to the tourniquet. Blood studies show a thrombocytopenia (100,000 or less), prolonged bleeding time, and normal clotting time but poor clot retraction. Some anemia due to blood loss and some leucocytosis are present. The disease need not be confused with hemophilia, which occurs only in males, with normal bleeding time, prolonged clotting time, good clot retraction, a firm clot, a normal tourniquet test, platelet count which is normal, and a history indicating the hereditary nature of the disease. Other diseases with which it may be confused are aplastic anemia, leucemia, and secondary purpura or symptomatic purpura.

Pseudohemophilia and chronic thrombasthenia are probably not the same entities. All blood studies may be normal, including clotting and bleeding time, yet bleeding continues. The diagnosis is made by exclusion. The spleen may be enlarged, usually much more than is seen in thrombocytopenic purpura, but splenectomy is definitely contraindicated because it will not help the disease and will be followed by continued bleeding. Splenectomy is usually curative. When it fails, an accessory spleen which has been overlooked should be thought of. This is not invariable, and in the acute variety bleeding may continue in spite of splenectomy. Just as thrombocytopenia is not always synonymous with the clinical features of the disease prior to splenectomy, so after the operation, although the platelets do not return to normal, the clinical symptoms, especially bleeding, subside. During a crises, surgery is best postponed. (We have had one patient in whom bleeding continued after splenectomy. No accessory spleens were found; there was generalized lymphadenopathy—perhaps an overactive reticulo-endothelial system.)

Thrombasthenia is a functional defect of platelets which predisposes the patient to repeated hemorrhage. It is probably related to thrombocytopenic purpura and may be suspected if the addition of normal platelets to the patient's deplateletized plasma corrects the coagulation defect (Alexander and Landwehr).

D. Combined Form.—Primary splenic panhematocytopenia is a disease due to hypersplenism in which most of the cellular elements of the bone marrow are destroyed, resulting in neutropenia, anemia, and throm-

Despite these facts, in prolonged crises, we have on several occasions given repeated small transfusions carefully cross matched, including the Rh factor, and at surgery large amounts of plasma followed by whole blood immediately after the splenic pedicle has been ligated, and our results have justified the cautious pursuance of this practice in selected cases. Gallstones should not be removed at the time of splenectomy.

2. Acute hemolytic anemia (Lederer) belongs to the group of intrinsic or idiopathic anemias characterized by fever, anemia, and splenomegaly. Splenectomy is of no value in the treatment of this disease.

3. Sickle-cell anemia is a familial disease occurring almost exclusively in Negroes. There is an anemia, the appearance of sickle-shaped red cells, and splenomegaly. The symptoms and signs are weakness, shortness of breath, abdominal crises with pain, splenomegaly for a while, joint pain and swelling resembling rheumatoid arthritis, leg ulcers, jaundice, and attacks of fever. Rarely there is vascular thrombosis which may occur in the cerebral vessels or elsewhere. Laboratory studies show sicklemia (which does not necessarily mean that the patient has the anemia) and anemia (normocytic type), some nucleated red cells, and leucocytosis with an increase in polymorphonuclears of all types, but also an absolute increase in eosinophiles, thrombocytosis. The sickle cells are best seen in moist preparations which have stood a while or are placed under a decreased oxygen tension. X-ray may show skull changes and osteoporosis of long bone. Splenectomy is indicated but is not curative. It is probably unwise to do this during a crisis.

Leucocytolytic.—Primary splenic neutropenia or idiopathic neutropenia is a disease of unknown origin in which the spleen destroys abnormally large numbers of neutrophiles to the exclusion of other cells. The reticuloendothelial cells of the spleen are engorged with polymorphonuclear neutrophiles as disclosed by supravital staining. The spleen becomes enlarged but is not adherent and is otherwise not characteristically affected. The patient complains of weakness, nervousness, and susceptibility to intercurrent infections. Leg ulcers are common; in fact, in our experience this symptom leads the patient to seek medical aid. The disease must not be confused with symptomatic agranulocytosis due to drugs, chemicals, or infections or aleucemic leucemia. Bone marrow studies are indispensable and will show no abnormalities or hyperplasia of granulocytic cells and no others. Splenectomy is definitely indicated and is curative.

Thrombocytolytic.—Thrombocytopenic purpura (Werlhof's disease, idiopathic thrombopenic purpura, purpura hemorrhagica) is an acute or chronic disease with a great reduction in blood platelets and bleeding from the mucous membranes with or without splenomegaly. It is a primary disease and not the secondary type of purpura which is seen in various types of infections, leucemias, chemical poisons, and nephritis. Girls and young women are affected much more frequently than boys or men. The disease has been ascribed to an increased avidity of the spleen for thrombocytes and/or a splenic extract which acts upon the bone mar-

in (1) Gaucher's disease, (2) erythroblastic anemia, (3) sickle-cell anemia. Splenectomy is not helpful in the infections except perhaps in some cases of abscess, the lipoid dyscrasias, cirrhosis of the liver, hemochromatosis, Still's disease and usually in Felty's syndrome, acute hemolytic anemia, the symptomatic erythremias. The operation should not be done in the lymphatic or lymphoblastic dyscrasias, primary erythremias, and most primary anemias. The operation of splenectomy has in the past carried a high mortality which has been variously estimated as 13 per cent in all cases and up to 34 per cent in those patients who are acutely ill. The chif dangers of the operation are hemorrhage, especially in Banti's syndrome, thrombosis of the portal vein with hepatic infarction, wound dehiscence, unrecognized pancreatic injury with subsequent leakage and fat necrosis, and injury to the diaphragm.

A few practical points concerning technique may be mentioned:

(1) The patient should be placed in the reverse Trendelenburg position on the table. (2) A cannula should be inserted in an ankle vein so that if large quantities of blood or plasma are necessary they may be given rapidly. (3) Incisions should be adaquate—they may be transverse, which is the best in smaller spleens; longitudinal, with left lateral extension; Bevan's Z incision, left paramedian; transthoracic through the bed of the eighth rib, which is useful in large spleens or in those adherent to the diaphragm. (4) The pedicle may be clamped first and this is preferable. In trauma with splenic tear, this should be done as quickly as possible, and the three-clamp method is best. The spleen is delivered by dividing avascular attachments; both vessels are clamped at once and cut between the two distal clamps. In very large spleens, malignant spleens, and those densely adherent to the diaphragm, the splenic artery should be tied close to its origin through the gastrohepatic omentum. After splenic massage or the injection of Adrenalin into the spleen to make it shrink, the vein is tied. Usually the splenic artery is tied through the gastrocolic ligament, then it is freed, and then the vein is ligated. (5) If the spleen is densely adherent to the diaphragm, the peritoneal covering of the undersurface of the diaphragm may be peeled with the adherent spleen instead of trying to separate it. (6) The pancreas should be carefully protected. Despite statements to the contrary, injury to the pancreas, if not recognized, may not only lead to fat necrosis, but also to wound dehiscence and deep abscess. (7) The spleen should be handled carefully so that splenic implantations do not occur through its rupture. (8) Accessory spleens should be sought and removed if found. (9) In certain desperate cases the splenic artery may be tied and divided.

THE ENDOCRINE GLANDS

The endocrine system (comprising the ductless glands or the glands of internal secretion) is only partially understood. However, rapid strides have been made within recent years. This group includes the pituitary (hypophysis); the pineal, the suprarenals or adrenals (which are compound organs and are the principal representatives of the two systems of glandular tissue called chromaphil and cortical systems, respectively); the carotid glands or intercarotid bodies (Chapter 14) (which are outlying parts of the chromaphil system); the thyroid, the parathyroids, and the thymus (which are developed from the entodermal lining of the embryonic pharynx); the spleen and the glomus coccygeum (which are associated with the circulatory system).

In addition, the liver, pancreas, gastric and intestinal mucous membrane, the kidney, testes, ovaries, and corpus luteum have internal as well as other secretions.

bocytopenia. The etiology is unknown, and the disease appears in an acute and chronic form, the latter with remissions and exacerbations. The diagnosis is difficult to establish, but in a case of splenomegaly with the foregoing blood findings, bone marrow studies should be made. These will usually disclose hyperplasia of the elements involved. Splenectomy is curative and should be done as soon as the patient can be prepared for surgery by repeated transfusion.

Group VII. Neoplasms and Cysts.—Neoplasms and cysts as outlined in this chapter are difficult to diagnose as such. In the presence of a large spleen, the diagnosis is made by exclusion and, in addition, bits of evidence which may be gleaned from a careful history and complete physical examination. Primary tumors cannot be recognized preoperatively except perhaps hemangioma, which gives rise to a bruit over the left hypochondrium. Huge cysts cause great distortions of x-ray patterns, and echinococcus disease may be suspected by complement fixation tests or skin tests. Secondary growths are more frequently correctly suspected because of the primary malignancy. Splenectomy is indicated, and because of this group a large spleen without definite contraindications should be removed.

Group VIII. Vascular Splenic Enlargements.—*Aneurysm* of the splenic artery is thought of in syphilis, after trauma, in arteriosclerosis, and in embolism. Pain and splenomegaly are the chief symptoms and signs. A bruit may be heard. Splenectomy should be done.

Arteriovenous fistula must be very rare but has been reported after wounds. The symptoms and signs are as in aneurysm, but, in addition, cardiac hypertrophy may occur together with other phenomena as outlined in Chapter 17. Splenectomy is indicated.

Embolism with infarction is not rare in the spleen. In subacute bacterial endocarditis the infarcts are infected, giving rise to splenic abscess which may undergo resolution or may receive splenectomy.

Thrombosis of the splenic vein has been discussed under Banti's disease. The acute varieties due to trauma or inflammation usually subside. Those due to pressure from neoplasms will not subside and wil require splenectomy when the primary lesion (pancreas, colon) is removed. Sometimes thrombosis occurs in polycythemia vera. We have seen several cases but decided not to do splenectomy. Resolution occurred.

Indications and Contraindications for Splenectomy

While no hard and fast rule can be laid down for the operation, the greatest benefits are derived in the following diseases: (1) traumatic lesions, whether by external force or tension, (2) abscess, (3) early splenic congestive splenomegaly due to portal obstruction and in all cases due to splenic vein obstruction, (4) hemolytic jaundice, (5) splenic neutropenia, (6) thrombocytopenic purpura, (7) splenic panhematocytopenia, (8) neoplasms and cysts, (9) aneurysm of splenic artery or arteriovenous fistula. Less striking results may be expected from splenectomy

capped by the small pars tuberalis), a pars intermedia, and a posterior pars nervosa. The anterior part and the pars intermedia come from an evagination of the ectoderm of the primitive buccal cavity, whereas the posterior pars nervosa and a portion of the intermedia come from the diencephalon. Some *fifteen* different functions have been attributed to it. Its anterior and posterior lobes have entirely different functions. The former controls growth and maturity; the latter, the *contraction of unstriped muscle.*

The anterior lobe secretes six hormones: (1) growth-stimulating, (2) thyrotropic, (3) adrenotropic, (4) and (5) *gonadotropic* (*follicle* stimulating and luteinizing), and (6) prolactin, or the lactogenic hormone. In addition, the anterior lobe has the following effects, *although no* separate hormones have been isolated: (1) ketogenic (causing a rise in acetone bodies), (2) hyperglycemic, (3) parathyrotropic, and (4) *pancreatropic (stimulating insulin production).*

The posterior lobe produces a pressor substance affecting unstriped muscle. This has a (1) circulatory effect, (2) plain muscle effect, (3) antidiuretic effect, and (4) metabolic effect (hyperglycemia, reduced sugar tolerance, reduced hepatic *glycogen,* and a fall in the basal metabolic rate). Two extracts have been obtained: *pitressin,* which raises blood pressure and is antidiuretic and affects *smooth muscle, and pitocin,* which contracts smooth muscle, especially uterine, and causes hyperglycemia. The only hormone produced by the intermediate lobe is *the melanophore—expanding* principle.

Pathological States of the Pituitary Gland.—

Anterior Lobe.—The chief cause of pituitary dysfunction is the presence of tumors (adenomas). There are two kinds: (1) chromophile adenomas (the cells of which accept stains), which usually cause hyperpituitarism, and (2) chromophobe tumors (the cells of which are not *easily stained*), which by pressure or destruction or altered secretion produce hypopituitarism.

In the group of chromophile adenomas there are again two types: (1) *Acidophilic adenomas,* which are made up of cells which accept an acid stain. If these occur in early childhood, they cause *gigantism; if* in later life, *acromegaly*—large, thick hands, big jaw, enormous tongue, and prominent cheek bones. (2) *Basophilic* adenomas which are made up of cells which take a basic stain. These seem to cause early or premature sex development.

Chromophobe adenomas inhibit the pituitary secretion, and if this occurs in childhood, there is an inhibition of maturity and sex development (*dystrophia,* adiposogenitalis—Fröhlich's syndrome), with deposition of fat. In the male there is a tendency to *female* characteristics, whereas in the female there is sex retardation and obesity, especially about the hips. *The lack of pituitary hormone* in infancy may cause *dwarfism,* producing small adults, normal except for size. *In adult life,* retrogressive sexual changes occur, with deposition of fat. In some forms of pituitary disease other glands *are also involved,* which makes the exact type impossible to diagnose.

Posterior lobe disease gives a confusing picture of polyuria (*diabetes insipidus*), hypertension, and overactivity of *the* parasympathetics. Diagnosis is made from the symptoms and signs, x-ray of the sella turcica, careful checking of *the eye grounds,* and examination by perimetry for bitemporal hemianopia, or obliteration of vision on the nasal half of each

In this chapter we shall consider briefly the pituitary, the pineal, the thymus, the thyroid, the parathyroids, the adrenals, the ovaries, and the testes. The function of the glands of internal secretion is to obtain a general effect. Nature uses the central nervous system for restricted, specific effects, the autonomic nervous system for broad, segmental effects, and the endocrines for widespread mass effect. A ductless gland liberates a hormone which does not affect the organ itself but has a general action. Small amounts of the hormone may be stored, but not for long. Therefore, the endocrine glands produce a continuous secretion.

A hormone is a chemical substance elaborated in one organ and carried by the blood stream to other organs and tissues, where it exerts a stimulating or retarding action. Glands do not produce secretions which act on themselves. If the secretion is introduced as substitution therapy, the gland may be stimulated or put at rest, but the effect is not on the gland.

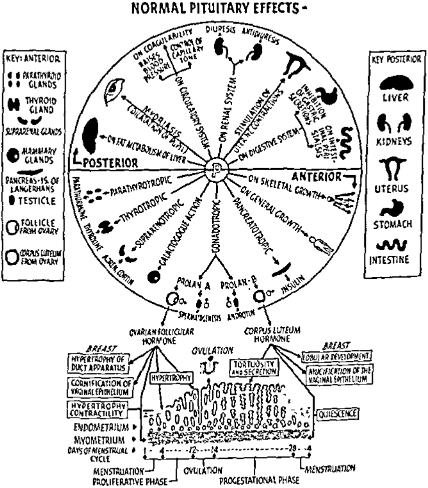

Fig. 382.—Diagram illustrating the normal effects of pituitary and ovarian hormones. Above are represented the pituitary effects and below, the ovarian hormonal activity. The ovarian follicular hormone is also known as folliculin (from the follicle), female sex hormone, theelin (Greek, female), progynon (Greek, before woman), oestrin (estrus-producing agent), menformon (monthly-acting principle), and estrogen. The corpus luteum hormone is also known as progestin, corporin, and progesterone. (Slightly modified from Gregory: A B C of the Endocrines, 1935, Williams and Wilkins Co., and Witherspoon: Clinical Pathological Gynecology, 1939, Lea & Febiger.)

The Pituitary Gland or Hypophysis

This small bilobed gland lies at the base of the brain on the sella turcica, immediately behind the optic chiasm. It is considered by many observers to be the principal gland of the endocrine system. It is composed of an anterior pars distalis (which is

Hypofunction of the pituitary due to chromophobe adenoma and hypopituitary cachexia (Simmond's disease) is accompanied by hypofunction of the thyroid, adrenal cortex, and gonads, as manifested by low basal metabolism, low blood pressure, excessive loss of sodium in the urine by hyponatriumemia, low blood sugar, genital atrophy, amenorrhea. The hypoglycemia was discussed previously in this chapter and was outlined as due to anterior lobe pituitary hypofunction caused by destructive lesions (chromophobe adenomas, cysts), atrophy and degeneration (Simmond's disease), thyroid hypofunction secondary to pituitary hypofunction.

Fig. 384.—Cushing's disease (pituitary basophilism). Basophilic adenoma of the anterior lobe of the pituitary. Note obese abdomen with (purplish) striae. This patient also had hypertension, osteoporosis, acne, polycythemia, frank diabetes, fatigue and changes in carbohydrate metabolism.

Posterior lobe deficiency causes *diabetes insipidus,* or is at least related to its cause. Other factors which have been mentioned as related to its cause are hyperthyroidism, pinealoma (through invasion of the hypothalamus and posterior lobe of the pituitary or involvement of the nerve tract from the hypothalamus to the pituitary which is known to produce the disease when cut or destroyed), and syphilis. The treatment is that of substitution therapy with posterior lobe extracts. Cures have

retina (see Chapter 18). A pituitary tumor, in other words, gives rise to local pressure effects on the brain and the sella (which may be eroded) and systemic hormonal effects as well.

Overactivity of the anterior lobe after maturity causes acromegaly; *before* maturity, gigantism; or it may cause a state of obesity in the trunk, face, and abdomen, with brittleness of the bones, hypertension, hyperglycemia, frank diabetes, changes in carbohydrate metabolism, polycythemia, fatigue, and glycosuria, and atrophy of the testes or ovaries (pituitary basophilism, or Cushing's disease). It is well to remember that certain groups of these symptoms, if not all, may be seen in (1) adrenocortical "hyperplasia," (2) adrenocortical tumors, (3) tumors of the thymus, (4) parathyroid tumors, (5) arrhenoblastoma of the ovaries. *Deficiency of the anterior lobe hormone* causes dwarfism in childhood, retrogressive sexual changes with deposition of fat, extreme emaciation, anemia, low metabolic rate, amenorrhea, and mental deterioration (Simmond's disease, or pituitary cachexia).

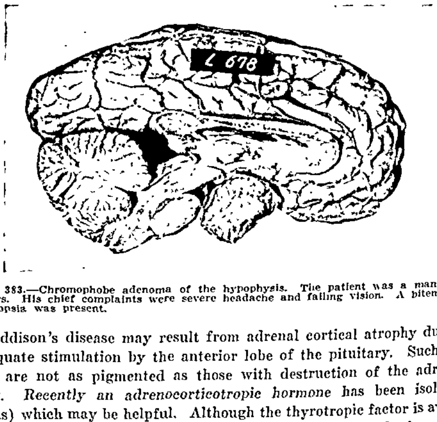

Fig. 383.—Chromophobe adenoma of the hypophysis. The patient was a man aged 44 years. His chief complaints were severe headache and failing vision. A bitemporal hemianopsia was present.

Addison's disease may result from adrenal cortical atrophy due to inadequate stimulation by the anterior lobe of the pituitary. Such patients are not as pigmented as those with destruction of the adrenal cortex. *Recently an adrenocorticotropic hormone* has been isolated (Evans) which may be helpful. Although the thyrotropic factor is available for clinical trial, its effects are evanescent and soon the hormone ceases to stimulate the thyroid gland. The gonadotropic hormone of the pituitary may be given in powder form and will in some cases stimulate the ovary so that menstruation and ovulation will occur where these functions have been absent. The hypothalamus plays a role in the release of the luteinizing hormone of the anterior lobe of the pituitary.

the frontal bone approach as well as the intranasal operation, in which the floor of the sella turcica is removed after a submucous resection, the latter has been largely abandoned now because of the dangers of meningitis. In deficiency states, pituitary extract is administered.

The Pineal Gland

The pineal gland lies on the roof of the third ventricle. It is very small but may be the seat of pinealoma, which may give rise to the symptoms and signs of a brain tumor. The function of the gland is said to be related to growth and sex development.

The Thymus Gland

The thymus gland is derived from each third pharyngeal pouch which toward the end of the sixth week begins to sacculate anteriorly. In the seventh week these sacs or pouches are detached and gradually descend into the mediastinum. The hollow

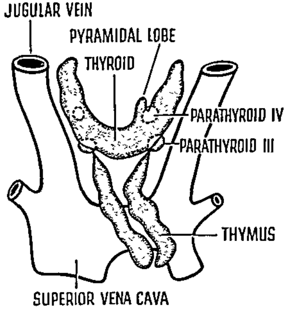

Fig. 386.—Glandular derivatives of the human pharynx. Diagram illustrating the thyroid, parathyroids, and thymi at two months in the ventral view. (After Verdun, ×15). (Redrawn from Arey Developmental Anatomy, Philadelphia, 1942, W. B. Saunders Co.)

pouches are attached to the pericardium at their lower ends, and the upper ends become stretched and thin and finally disappear. By the tenth week the thymic corpuscles appear. They are probably masses of reticulum cells, and by the third month lymphoid tissue has formed and the gland differentiates into cortex and medulla. Lymphocytes then migrate into the bilobed gland from without. The thymus enlarges until puberty, then regresses. Congenital anomalies occur. The upper ends of the thymus may persist, either continuing the thymus from the thyroid down or as separated accessory thymus lobes at the inferior margin of the thyroid. Rarely the thymus originates from the fourth pouch, giving rise to aberrant lobes.

The thymus gland lies in the lower part of the neck and in the superior and anterior mediastina. It is relatively large in infants and may, by pressure, produce

been reported following simple lumbar puncture, x-ray therapy to the pituitary, total thyroidectomy, and x-ray treatment of pinealoma or surgical removal.

Other tumors in the pituitary are: (1) The adamantinomas which occur in children and give the same symptoms as the chromophobe adenomas. X-ray shows calcium deposits and an enlarged sella. (2) The suprasellar cysts which originate in Rathke's pouch and are not rare in children. The cyst may arise anywhere along the stalk. The symptoms and signs are variable. If the cyst is in the upper infundibulum, symptoms of increased intracranial pressure are present; if in the lower part, bitemporal hemianopsia may be present. Choked disc and primary optic atrophy are common. The treatment is surgical excision.

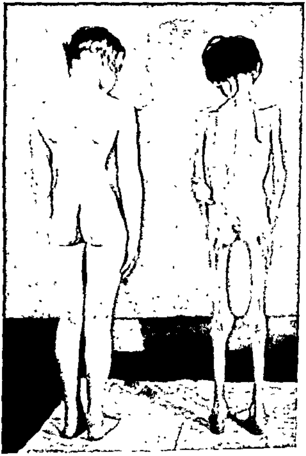

Fig. 385.—Simmond's disease (pituitary cachexia). A normal child of the same age (nine years) is shown on the left. The patient had many attacks of illness from the age of three years. At the age of eight years she had severe attacks of vomiting and diarrhea, with rapid weight loss and extreme emaciation. The patient could stand but not walk, mentality was normal. Blood pressure: 75 systolic, 45 diastolic. Blood sugar range: 60 to 106 mg. The response to anterior pituitary extract was poor and death occurred three months after release from the hospital.

Since anterior lobe dysfunction is usually due to an adenoma, the treatment is the surgical removal of the growth if possible; if not, x-ray therapy is used. The name of Harvey Cushing is indelibly associated with the description and removal of these growths. Although he used

Thymus Enlargements.—The thymus has been found to be enlarged in myasthenia gravis. Moreover the disease is helped by x-ray treatment of the thymus. These observations have led to the performance of thymectomy in selected cases of myasthenia gravis. The gland is difficult to reach. The most direct approach is through the sternum. This is split down the center to within two inches of the xyphoid-sternal junction and then cut transversely, which permits bilateral retraction. A second method is the division of the third and fourth costal cartilages with resection of two to three inches of these structures, and then by incising the perichondrium vertically, the mediastinal pleura may be retracted laterally and the thymus removed. The internal mammary artery is doubly tied and divided. A third approach is the transthoracic one. This is useful in large growths and may be supplemented where necessary by removing a portion of the sternum. Usually the approach is through the bed of the fifth rib.

The Thyroid Gland

The thyroid gets its name from "shield." It is a ductless gland that has two lobes which lie on either side of the trachea and are connected by an isthmus. This lies in front of the trachea just below the cricoid cartilage. The gland tissue is arranged in little units (*acini*), the walls of which are formed by low cuboidal cells, and the lumen of which is filled with a clear, homogeneous, iodine-containing substance known as *colloid*. These irregular sacs or acini are surrounded by connective tissue and blood vessels and lymphatics.

Embryology.—

The thyroid appears as an invagination of the mid-ventral wall of the pharynx in the fourth week of fetal life, between the first and second branchial arches. This constricts off and forms a stalked vesicle. The stalk is the thyroglossal duct. Should this duct fail to obliterate, a cyst forms (thyroglossal duct cyst), which may appear in the midline anywhere from the foramen cecum of the tongue to the isthmus. Aberrant thyroid tissue may be found at the base of the tongue or under the sternomastoid muscles. In the former position this represents all of the thyroid tissue present; in the latter, it is potentially malignant.

This aberrancy is produced by four factors: (1) The median factor may give rise to a pyramidal lobe which results from the retention and growth of the lower end of the thyroglossal duct. (2) The lateral factors are the ultimobranchial bodies which are joined with the adjacent parathyroid IV and set free from the pharynx at about the seventh week. Meanwhile the growth of the thyroid brings its two lobes into contact with the ultimobranchial bodies and the latter disappear or are converted (due to influence of the thyroid environment on a plastic implanted tissue—Arey) into thyroid tissue. Sometimes these "thyroid primordia" remain in a lateral detached position. (3) Malmigration—this factor may cause the thyroid to enter the chest or remain at the foramen cecum as a lingual thyroid. (4) Heterotopia or ectopia—thyroid tissue may be found in the ovary (struma ovarii) or other unpredictable location.

Anatomy.—Beneath the skin are the panniculus adiposus (superficial fascia) and then the panniculus carnosus (platysma). The "ribbon muscles" of the neck (sternohyoid and sternothyroid) lie immediately in front of the capsule. The deep fascia (fascia Colli) may be looked upon as a fibrous sheath which dips in and out of

some interference with breathing (thymic asthma), although this concept is now disputed. This condition is treated by x-ray, which reduces the size of the gland. After *puberty the thymus normally undergoes gradual involution.*

In the neck the gland *lies behind the sternohyoid and sternothyroid* muscles and anterior to the trachea. In the thorax it is covered by the sternum, to which it is attached, and below it is separated from the aortic arch, pericardium, and large vessels by *a thin fascial layer.* Its blood vessels come from the superior and inferior thyroid and internal mammary arteries. Its veins *empty into the thyroid, internal mammary,* and innominat eveins. Its capsule has nerve fibers from the phrenic and descendens hypoglossi, whereas the gland contains branches of the sympathetic and parasympathetic fibers (vagus).

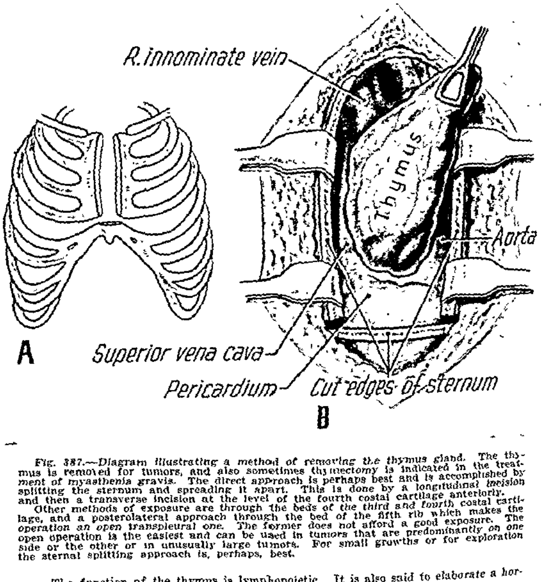

Fig. 387.—*Diagram illustrating a method of removing the thymus gland.* The thymus is removed for tumors, and also sometimes *thymectomy* is indicated in the treatment of *myasthenia gravis.* The direct approach is perhaps best and is accomplished by splitting the sternum and spreading it apart. This is done by a longitudinal *incision* and then a transverse incision at the level of the fourth costal cartilage anteriorly.

Other methods of exposure are through the beds of *the third and fourth* costal cartilage, and a posterolateral approach through the bed of the fifth rib which makes the operation *an open* transpleural one. The former does not afford a good exposure. The open operation is the easiest and can be used in tumors that are predominantly *on one* side or the other or in unusually large tumors. For small growths or for exploration the sternal splitting approach is, perhaps, best.

The function of the thymus is lymphopoietic. It is also said to *elaborate a hormone* which affects *growth and maturation.* The *so* called status thymicolymphaticus, or state in which sudden death in a child has been attributed to an enlarged thymus, probably does not exist.

ate abduction (due to stimulation) and *loss of voice except for a whisper.* Eventual fibrosis of the vocal cords, together with fixation of the arytenoids, results in great narrowing of the glottic space, *making breathing difficult on the slightest exertion.* Injury to one nerve is not so serious because the opposite cord compensates for the inactivity of the injured side.

The thyroid, as seen in microscopic sections, is made up of acini lined with low cuboidal epithelium and filled with colloid. This epithelium becomes enfolded and the cells enlarge, becoming columnar, when hypertrophy and hyperplasia occur. Williamson believes the thyroid to be composed of a number of lymphatic sinusoids, in which are suspended epithelial cords or cylinders. Rienhoff describes the gland as made up of follicles which are not entirely separated from one another by a complete covering of connective tissue. The latter forms a continuous fenestrated meshwork, which grows in from the capsule. The parenchyma is continuous throughout.

Physiology.—

1. *The Relation of the Thyroid to Other Endocrine Glands.*—The thyroid is influenced by the pituitary (through the thyrotropic hormone), by the adrenals (perhaps inhibitory through the pituitary), and by the gonads. The influence of the gonads is very important and is observed clinically during puberty, menstruation, and pregnancy. Often thyroid activity is increased following surgical removal of the ovaries, or at the menopause. In animals, castration leads to reduction in size of the thyroid and depression of the metabolic rate, while the continued injection of estrogenic hormones causes thyroid enlargement, followed by involution. Thyroid feeding inhibits estrus. Menstruation is reduced or absent in thyrotoxicosis. It is increased in myxedema. The pituitary is influenced by the thyroid specifically and by a calorigenic effect. Total thyroidectomy causes hypertrophy of the pituitary, and subtotal thyroidectomy is not followed by compensatory hyperplasia in hypophysectomized animals, a fact which has led to the treatment of hyperthyroidism by x-ray exposure over the pituitary. The adrenal medulla is definitely related to the thyroid. The exaggerated sensitivity of patients with hyperthyroidism to epinephrine is suggestive of its underfunction in this disease. The pancreas and the thyroid may be antagonistic, but the deleterious effect of the severity of diabetes mellitus may not be due to an antagonism between the thyroid and insulin but may be due entirely to the increase in metabolism in hyperthyroidism, which demands more glucose, which in turn is incompletely metabolized due to deficient insulin. We have already observed, in our discussion of hypoglycemia, that the thyroid, pituitary, pancreas, and adrenals are related to sugar metabolism.

2. *Iodine Metabolism and the Thyroid Hormone.*—The thyroid hormone has many interrelated effects; the more prominent are as follows: (1) The regulation of heat production or its equivalent oxygen consumption and carbon dioxide production; that is, the rate of energy exchange or metabolism (calorigenic action). The basal metabolic rate is below normal in starvation and undernutrition, in obesity due to pituitary or hypothalamic disorders, in hypothyroidism, in Addison's disease, in lipoid nephrosis, and in shock. It is above normal in hyperthyroidism, fever, diabetes insipidus, cardiorenal disease with dyspnea, leucemia, and polycythemia. (2) the effect on growth maturation and differentiation of tissue. (3) The distribution of water, salts, and colloids of the body are affected. In hypothyroidism there is a storage of water, salts, and protein. In myxedema the so called "deposit protein" is stored in the body fluids and is quickly oxidized and excreted through the urine when the thyroid is administered. This diuresis is caused by a loss of intercellular fluid is evidenced by the urine's high content of sodium salts. Myxedema is due to the abnormal collection of mucoprotein derived from the cell's ground substance. Myxedematous tissue resembles fetal tissue in its high mucin content. Does this mean that the thyroid provides for a "mature" environment for tissue cells? (4) Carbohydrate metabolism is affected. Glycogen in the liver is depleted in hyperthyroidism and increased in hypothyroidism. Diabetes is aggravated in the former and is less severe in myx-

the principal structures of the neck, forming their covering. The superficial layer encloses the sternomastoid muscle and forms two layers which are attached in front and behind the sternum. The pretracheal layer ensheathes the thyroid and then continues around in front of the prevertebral muscles. Laterally it blends with the carotid sheath, which is also a special part of the cervical fascia. The prevertebral layer lies in front of the prevertebral muscles. The sheath of the thyroid is therefore a part of the pretracheal fascia. This same layer is attached to the larynx, trachea, and esophagus, causing the thyroid to move with swallowing. Behind the sheath lie the parathyroids and the recurrent laryngeal nerve. The latter runs along the groove between the trachea and esophagus. Injury to this nerve causes adductor and abductor paralysis. Removal of the parathyroids causes tetany. The capsule of the thyroid is closely adherent and sends supporting fibrous septa into the stroma. The deep cervical fascia is therefore really composed of two strong sheets, which are attached on the lateral side of the neck, dividing it into three compartments: a posterior or vertebral, containing the muscles of the spinal column, a middle or visceral, containing the great vessels, the esophagus, the pharynx, and the thyroid, and an anterior or muscular, containing the sternomastoid and ribbon muscles.

The normal thyroid weighs about 25 to 40 grams and is a very vascular organ, receiving its blood supply from the superior and inferior thyroid arteries (from the external carotid and thyrocervical trunks, respectively) and often the thyreoidea ima (from the aorta or innominate). If a pyramidal lobe is present, it gets its blood supply from the superior thyroid, usually the left by a special branch. There is a prodigious amount of anastomosis, and the superior and inferior thyroid arteries communicate through an anastomosing trunk on the posterior aspect of the lateral lobes. This trunk is a guide to the parathyroids. Three pairs of veins drain the gland unless accessory veins are present. Typically the upper two, the superior and middle thyroid veins, empty into the internal jugular; the lower or inferior thyroid veins join as a trunk which empties into the left innominate. The veins cover the surface of the gland anteriorly and over the trachea and anastomose freely across the isthmus. The lymph vessels drain into the deep cervical and pretracheal nodes.

The nerve supply comes from the middle and inferior cervical ganglia of the sympathetics and accompanies the blood vessels. In the operation of thyroidectomy, adjacent nerves are encountered which do not supply the thyroid gland but must be recognized. These are the superior laryngeal and the recurrent laryngeals, both branches of the vagus. The former have two branches, an internal, which goes through the thyrohyoid membranes, supplying the mucous membrane of the larynx, and an external, which passes down on the inferior constrictor muscles of the pharynx, supplying this muscle and the cricothyroid. It may be injured in dealing with the superior pole. The recurrent laryngeals are far more important. The right arises from the vagus as it crosses the first part of the subclavian artery. It hooks around the artery, then passes upward and medially behind the subclavian and the common carotid, then more medially behind the inferior thyroid artery and thyroid gland in the interval between the trachea and esophagus. On the left the nerve leaves the vagus as it crosses the aortic arch, which it hooks around lateral to the ligamentum arteriosum, then follows a course similar to the right. Great variations occur in its course upward. The nerves may (1) differ on each side; (2) ascend anterior to the inferior thyroid artery; (3) not descend but cross at a high level and enter the larynx directly; (4) descend to the inferior thyroid artery, then ascend to enter the larynx; (5) hook around the inferior thyroid; (6) divide into abductor and adductor branches at various levels outside the larynx. The importance of these facts becomes even more practical in the surgical treatment of goiter, because the nerve may be compressed against the trachea or into abnormal positions of all sorts. The nerve carries both abductor and adductor fibers, thereby carrying impulses which produce opposing muscle actions of the vocal cords; namely, abduction and adduction. In addition, coordinated impulses are carried which are concerned with speech and breathing. Severance of both nerves results in immedi-

Blood iodine is about 8 to 10 micrograms per 100 c.c. of blood. A small amount of this is due to inorganic iodine, representing exogenous material (nutrition, medication); the rest is due to organic iodine and may represent the amount of circulating hormone. The concentration of iodine fluctuates with diet, exercise, medication, seasons. It is low in myxedema and high in thyrotoxicosis.

The hormone is secreted in two ways: (1) Directly into the blood stream (and this is the predominant way in hyperthyroidism) and (2) into colloid. The normal gland does both—colloid is probably formed in the follicles by action of the cells in four stages, namely, secretion, colloid release, partial collapse, and recuperation, very much as apocrine glands behave elsewhere. Just how colloid gets into the blood stream is unknown, or how thyroglobulin (which has a molecule) diffuses across a living semipermeable membrane is unknown. Perhaps by enzymatic action it is partially broken down into smaller molecules.

The gland then is an independent factory and sets up its own metabolism based upon available iodine, body needs, and other factors. Since thyroxine must be doled out continuously, a store of this material is always available in the colloid unless in abnormal states, where thyroxine is removed as fast as it is made—but in the normal gland a certain amount of thyroid hormone is given to the body and the rest is stored in colloid *to be used as needed. Goiter results if iodine is lacking* when there is an increased demand for thyroxine. Iodine reaches the thyroid as iodide. The thyroid cell changes this and produces a protein thyroglobulin, in which the iodination of tyrosine and subsequent formation of thyroxine takes place. Thyroglobulin is the protein in which thyroxine is stored in the gland. When thyroglobulin splits down as a result of thyrotropin stimulation, thyroid hormone is delivered into the blood stream. The rate of thyrotropin stimulation is set by the amount of thyroid hormone in the blood.

The good effect of iodine in goiter is probably due to endothelial damage by the iodine. Since blood iodine is high in thyrotoxicosis and gland iodine is low, and since this is reversed during remission, we may deduce that the thyroid capillaries leak thyroxine during the exacerbation stage. When the capillaries are sealed, iodine is retained, allowing the gland to store some as colloid. This is the picture seen in remission.

The height of the cells surrounding the acini is related to the amount of colloid which is present. They are cuboidal if much colloid is present, columnar if little is stored. The maximum storage capacity of the gland for iodine is about 5 mg. per gram of dried gland or about 25 to 40 mg. for the normal gland. Whenever the iodine content falls below 1 mg., hyperplasia occurs.

The extractable hormone of the thyroid is iodothyroglobulin. From it, thyroxine is extracted which has most of the pharmacological properties of iodothyroglobulin and is a derivative of di-iodotyrosine. Thyroxin is an integral amino acid which is elaborated at the rate of 0.3 mg. (0.2 mg. of iodine) per day. Tissues other than the thyroid probably are able to elaborate a thyroidlike substance—a condition present in lower forms in the phylogenetic scale.

3. *The Antithyroid Goitrogens.*—These are divided into two classes:

A. Those that act without producing goiter.

(1) Iodine causes a decrease in the size of the gland with deposition of colloid or the return to a resting phase. In toxic goiter whole blood iodine and precipitable serum iodine levels are higher, whereas the iodine content of the thyroid gland is less. With the administration of iodides, blood and serum iodine levels decline and the iodine content of the thyroid increases. This is indicative of lessened thyroid activity and is usually accompanied by a decrease in thyroid hyperplasia.

(2) Radioactive iodine is prepared in a cyclotron by nuclear bombardment of metallic tellurium that becomes transmitted into iodine. This is then dissolved, distilled, and reduced to sodium iodide. The dosage is about 0.5 to 1 mc. of 12 hour iodine per gram of estimated thyroid; 25 to 50 mc. radioiodine causes fibrosis of the gland.

edema; in fact, total thyroidectomy has been suggested for the relief of intractable diabetes. (5) The action on the nervous system is seen in hyperthyroidism with emotional instability, increased irritability, and psychosis, and the reverse more or less in myxedema, although irritability is present. (6) The muscular system is influenced by the thyroid as seen in hyperthyroid states where changes may vary from mild myasthenia to advanced muscular atrophy. Hypotonicity is present in hypothyroidism. (7) The circulatory system is affected through the other effects already mentioned plus increased cardiac irritability in hyperthyroid states and lowered tone in myxedema. (8) The metabolism of vitamins and other foods are regulated by the thyroid. When the rate of metabolism is high, food and vitamin requirements increase, especially proteins and vitamins B and C. (9) Exophthalmos, though frequently associated with hyperthyroidism, is probably not caused by the hormone per se. It is said to be due to the thyrotropic hormone of the pituitary which produces edema and cellular reaction in connective tissues of the body, including the retrobulbar tissue. Exophthalmos is more often associated with myxedema (resulting from postoperative, inflammatory, or spontaneous causes) than with hyperthyroidism. In such cases there is a myxomatous infiltration of the ocular muscles and retro orbital fat, crowding the eyes forward. Other theories are as follows: A true spasm or contraction of Mueller's muscle may be the cause, or it may be due to edema behind the orbit, which occurs due to the dilatation of the orbital venules and the absence of lymphatics in this region to absorb the edematous fluid. Exophthalmos may be increased following thyroidectomy. This may be explained on the basis of increased retrobulbar edema due to ligation and division of vessels. There may also be pseudohypertrophy of ocular muscles with edema degeneration and lymphocytic infiltration. This is explained as follows: The normal thyrotropic hormone stimulates the thyroid to produce thyroxin in sufficient quantity to meet the demands of the body. The thyroid uses up all of the thyrotropin, and pituitary inhibition results. Only small amounts of thyrotropin reach other tissues. In exophthalmic goiter there is excessive thyrotropin in spite of excessive thyroid inhibition. Much thyrotropin reaches the orbit, causing edema of the ocular muscles which weakens their inward pull; this, coupled with an increase of outward push by the edema in the fat and connective tissue, causes the exophthalmos. Exophthalmic ophthalmoplegia is a term used to describe exophthalmos and loss of ocular movements. It may be caused by excessive thyroxin or thyrotropin or both.

A temporary increase in exophthalmos may occur after thyroidectomy. This usually subsides and improvement continues until the eyes are almost normal, although the process may require one to two years. Increasing exophthalmos after thyroidectomy may be anticipated in those patients with mild symptoms and low basal metabolic rates. Some have advised medical treatment or x ray therapy in such cases to avoid this troublesome complication. Should exophthalmos continue with increasing lid pressure, the eyes may be lost due to local chemosis and ulceration. Such cases may be helped by unroofing the orbital canal and incising the orbital periosteum permitting the bulging of retro-ocular fat and muscles (Naffziger). Strabismus may remain in the ordinary case of exophthalmos after thyroidectomy if the eye bulge has been present for a long time. This is corrected by shortening or "tucking" the muscles.

Unilateral exophthalmos may be an early sign in exophthalmic goiter. One usually thinks of other causes for this finding such as (1) intraorbital inflammatory disease (primary or secondary due to paranasal sinusitis), (2) paralysis of extraocular muscles, (3) cavernous sinus thrombosis, (4) congenital anatomical defects, (5) angiomas or aneurysms within or below orbit, (6) neoplasms within or behind orbit.

Every thyroid gland varies in its iodine content from time to time and is affected by seasons, locality, and food habits. Normally about one-third to one-fourth of the total iodine of the body is in the thyroid. The dried gland contains about 0.186 per cent of iodine but varies from 0.05 to 0.45 per cent. Iodine is present in fetal thyroids as early as the third month. The iodine store varies inversely with the degree of hyperplasia.

(3) Thiouracil, propyl thiouracil, methyl thiouracil, thiourea, and the sulfonamides produce goiter by pituitary stimulation and not from direct action by these compounds on thyroid parenchyma. These drugs cause nearly complete disappearance of iodine from the thyroid gland in five days. They therefore interfere with the incorporation of iodine into tyrosine and di-iodotycosine, and formation of thyroxin in the thyroid gland, and thereby cause cessation of hormone synthesis. In addition to preventing iodination and hormone synthesis, they may act as antitoxidants through depression of the enzyme systems. Propyl thiouracil is usually given in doses of 200 to 300 mg. daily, depending on the toxicity of the patient. Toxic reactions include agranulocytosis, sore throat, fever, skin rash, gastrointestinal disturbances, and joint pains. In toxic goiter after the administration of these drugs, blood iodine as well as the amount of iodine in the thyroid gland decreases. When thiouracil is given for toxic goiter, particularly the diffuse hyperplastic type (Grave's disease), there results extreme hyperplasia with heightened epithelium, papillary infolding, and mitosis of epithelial cells.

Abnormalities of Function of the Thyroid Gland

Hypofunction may be (1) primary or (2) secondary. *Primary hypofunction* includes (a) cretinism, which may be sporadic or endemic, (b) hypothyroidism with or without myxedema which may be spontaneous, postoperative, postinfectious, postantithyroid drug administration. Secondary decrease in thyroid activity is seen in hypopituitarism and Addison's disease.

Hyperfunction is seen in hyperplastic (exophthalmic diffuse symmetric) goiter, in nodular toxic goiter (toxic adenoma), and in mixed types.

Congenital Anomalies of the Thyroid Gland

The thyroid may be entirely absent, giving rise to cretinism, or it may be present in various abnormal locations, such as behind the sternum (substernal), in the chest (intrathoracic) or mediastinum, at the base of the tongue (lingual), in the sides of the neck (lateral aberrant thyroids), or in teratomas anywhere (mediastinal, ovarian). Sometimes the thyroglossal duct persists as a sinus, a fistula, or a cyst (see Chapter 15).

Cretinism may be sporadic or endemic, the latter as an end result of untreated endemic goiter lasting over a period of several generations. *Sporadic* cretinism appears in the children of normal parents. Cretinism is myxedema in childhood. Thyroid extract is specific if given early before irreparable brain damage has occurred.

Substernal thyroid may result from *overmigration* of thyroid tissue but is frequently seen in goiter which may have plunged into the superior mediastinum during its enlargement, guided by the middle or visceral compartment of the deep cervical fascia. Its blood supply comes mostly from the inferior thyroid artery, but this is variable, and therefore in its extirpation all vessels are ligated prior to its extraction from the thorax.

Substernal goiters may be complete, with no thyroid tissue above the level of the suprasternal notch; intermittent, which refer to those which are small enough to slip into and out of the anterior compartment of the superior mediastinum; and combinations, in which part of the goiter

B. Those that cause an increase in size of the thyroid gland.

(1) Cyanides (found in cabbage) produce an iodine-deficiency goiter since it can be prevented by giving iodine.

(2) Thiocyanates prevent the synthesis of thyroid hormone at some point distal to the uptake of iodine since the thyroid continues to take up radioactive iodine. The administration of desiccated thyroid prevents or relieves thyocyanate goiter. Thiocyanate goiter resembles neoplasia.

Fig. 388.—Cretin. Clinical photograph of a cretin 8 years of age who has failed to grow or develop physically or mentally. She had not learned to walk, although her mental age was that of a 2-year-old. She presented the following characteristics and findings: weight, 27½ pounds; height, 31 inches; hair scanty and coarse; anterior fontanel open, measuring 3½ cm. in diameter; parietal sutures also open in the anterior portion. head large in proportion to the body; a nonpitting edema over entire body; tongue is thick, and the twenty teeth all deciduous; heart enlarged, and there is a systolic murmur, heard best over the apex; abdomen usually distended; an umbilical hernia is present. X-ray examination of the chest showed cardiac enlargement to the right and left of the midline. There were only two centers of ossification among the carpal bones, whereas normally there should be at least eight. Blood cholesterol was 457 mg. The child was given thyroid extract, ½ grain, three times a day and vitamin B complex.

(3) Thiouracil, propyl thiouracil, *methyl thiouracil, thiourea,* and the sulfonamides produce goiter by pituitary stimulation and not from direct action by these compounds on thyroid parenchyma. *These drugs cause nearly complete disappearance* of iodine from the thyroid gland in five days. They therefore interfere with the incorporation of iodine *into tyrosine and di-iodotycosine,* and formation of thyroxin in the thyroid gland, and thereby cause cessation of hormone synthesis. In addition to preventing iodination and hormone synthesis, they may act as antitoxidants through depression of the enzyme systems. Propyl thiouracil is usually given in doses of 200 to 300 *mg. daily, depending on the toxicity of* the patient. Toxic reactions include agranulocytosis, sore throat, fever, skin rash, gastrointestinal disturbances, and joint pains. *In toxic goiter after* the administration of these drugs, blood iodine as well as the amount of iodine in the thyroid gland decreases. When thiouracil is given for toxic *goiter, particularly the* diffuse hyperplastic type (Grave's disease), there results extreme hyperplasia with heightened epithelium, papillary infolding, and mitosis of epithelial cells.

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is in the neck and part has been pushed *down into the mediastinum*. The symptoms and signs of these goiters in addition to their general effects, if any, are those due to local pressure. These may include difficulty in

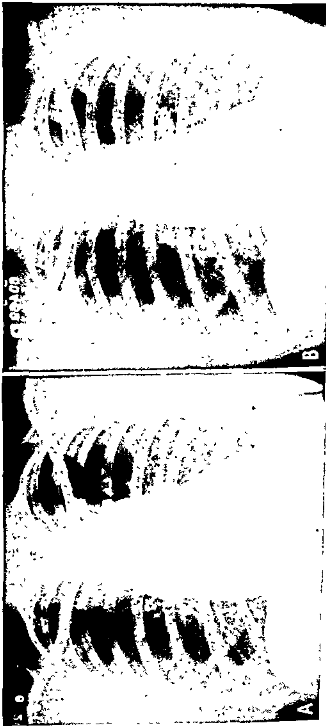

Fig. 389.—X-ray picture of a large intrathoracic "plunging" goiter. The patient was a woman aged 36 years. There was increasing dyspnea, and finally orthopnea, hoarseness, and dysphagia. *A*, Before operation. *B*, After operation.

breathing or swallowing, edema of the face and neck, and pain. In addition, there may be great dilatation of superficial veins of the upper chest and neck due to superior vena caval pressure and hydrothorax.

Diagnosis is made by the symptoms and signs and x-ray studies. The treatment is thyroidectmoy, and this is done through the classical collar incision and after the blood supply has been controlled. If the goiter is too large to be delivered, its capsule may be opened and the growth removed in part; then the capsule may be "peeled" out.

Intrathoracic or *mediastinal* thyroid is due to an overmigration or heterotopia or the inclusion of thyroid tissue in teratomas. Goiters have been found as low as the diaphragm (goiter *plongeant* from *plonger*—a descending or sloping part). Mediastinal goiters do not have the normal relationship to the carotid sheath, the trachea, and esophagus and do not get their blood supply from the thyroid arteries except rarely from the thyroidea ima. Their symptoms and signs are those of a mediastinal tumor (Chapter 20), and the diagnosis is made in the same way as in the care of these neoplasms. The treatment is their surgical removal through a thoracotomy. Thyroids have been found in the trachea and esophagus.

Lingual thyroid is more common than nasopharyngeal, intralingual, sublingual, and prelaryngeal, all of which illustrate a lack of descent of the thyroid tisue to its normal position. Lingual thyroid may be accessory thyroid tissue in addition to the normal gland. In lingual goiter, however, the thyroid at the base of the tongue between the epiglottis and circumvallate papillae is the only thyroid tissue present. The goiter is usually of the adenomatous type and is nontoxic. The symptoms and signs are due to the pressure of a tumor at the base of the tongue which interferes with swallowing, breathing, and speech. In addition, ulceration and infection due to trauma may cause bleeding. Differential diagnosis includes adenoma, angioma, fibroma, lipoma, and nonthyroid cysts; also sarcoma, lymphosarcoma, and carcinoma which may be associated with lingual goiter. Treatment consists of surgical removal either through the oral cavity or, rarely, through the neck in extremely large growths, after preliminary tracheotomy. In small growths transfixion sutures are used before removal, and in larger tumors the lingual arteries are tied. The most common postoperative complication is myxedema. This occurred in the two cases we have seen.

The lateral aberrant thyroids have been explained as arising from the fifth branchial pouch (ultimobranchial body) or from early separation of the aberrant tissue from the main body of the thyroid. These thyroids are usually multiple and are located in front of the sternomastoid muscle beside the internal *jugular vein*. Sometimes they are single. On microscopic examination they resemble a papillary cystadenoma, which, indeed, they are, but of the thyroid, and with the same malignant tendencies as papillary cystadenoma of the breast or ovary or other glandular organs There are few symptoms and signs except for the swelling in the neck They must be differentiated from midline thyroid tumors (undescended thyroids, pyramidal lobe, adenoma of the isthmus, thyroglossal duct cyst) and lateral tumors which are single (branchial

cysts, carotid body tumors, neurofibromas) and multiple (lymph node swellings, inflammatory or malignant, Chapter 17). Treatment consists of surgical extirpation, including the internal jugular vein, overlying muscle, lymph nodes, submaxillary gland, and the thyroid lobe on the affected side if the biopsy of any of the aberrant tissue is malignant. This is followed by x-ray therapy. If not malignant, simple removal is all that is required. Many so-called lateral aberrant thyroid tumors are really metastatic extensions to the deep cervical lymph nodes from a primary carcinoma in the homolateral lobe of the thyroid gland.

Thyroid tissue in *teratomas* has been reported. Their discovery is usually fortuitous, although in the presence of all of the classical symptoms and signs of toxic goiter after thyroidectomy aberrant thyroid tissue activity may be thought of.

Goiter

Not all enlargements of the thyroid gland are of the same nature, even though they are all called "goiter." Therefore, below will be found a simple classification of goiter. First in this list is the so-called *simple goiter.* The thyroid gland is frequently called upon to secrete an increased amount of its hormone (thyroxin). To do this it may undergo hypertrophy, hyperplasia, or both. Having met the emergency, it may return to normal, or it may go into a resting stage (acini filled with colloid), or it may undergo incomplete involution, or it may atrophy. Should it remain enlarged, with or without an excessive or perverted secretion, it forms a goiter. The most common causes for a simple goiter are *compensatory hypertrophy and hyperplasia.* This simply means that the thyroid gland has enlarged, in both the number and size of its cells, to meet an emergency. The smooth fullness in the necks of adolescent girls is a physiological enlargement. In some women this enlargement takes place with every menstrual period; in others, during pregnancy or during the menopause, or in any mental or physical stress or strain. These are all physiological causes of enlargement which is usually relieved by the use of iodine. This condition having occurred, the gland usually lapses into one of three states: (1) normal, (2) colloid rest stage, or involution, (3) atrophy of exhaustion.

During adolescence the body changes and grows rapidly and there is need for increased energy and metabolism. When the increased demand is over, the thyroid gland returns to normal. The same is true during periods of nervous stress and strain.

Classification of Goiter

A. Simple goiter (nontoxic)
   1. Compensatory hypertrophy and hyperplasia, due to physiological causes or acute infections
   2. Simple colloid goiter
      (a) Endemic
      (b) Result of previous hypertrophy and hyperplasia

3. Simple adenomatous goiter
   (a) Diffuse adenosis
   (b) Fetal adenoma
   (c) Combinations

B. Toxic goiter (thyrotoxicosis or hyperthyroidism)
   1. Exophthalmic—acute (crisis) or chronic
      (a) Diffuse hyperplasia
   2. Toxic adenoma (nodular toxic goiter)
      (a) Diffuse adenomatosis
      (b) Fetal adenoma and areas of hyperplasia

C. Infections
   1. Acute thyroiditis—suppurative and nonsuppurative
   2. Chronic thyroiditis
      (a) Riedel's struma (ligneous thyroiditis)
      (b) Struma lymphomatosa (Hashimoto's lymphoid struma)
      (c) Tuberculous thyroiditis
      (d) Syphilitic thyroiditis
      (e) Chagas' disease (*Trypanosoma cruzi*)
      (f) Amyloid disease resulting from infection elsewhere

D. New growths
   1. Benign
      (a) Cysts
      (b) Adenomas
         (1) Embryonal
         (2) Fetal
         (3) Colloid
         (4) Papillary
      (c) Fibroma
      (d) Endothelioma
      (e) Plasmacytoma
   2. Malignant—carcinoma
      (a) Primary carcinoma
         (1) Malignant adenoma
         (2) Papillary
         (3) Adenocarcinoma
         (4) Diffuse carcinoma (small-cell)
         (5) Giant-cell carcinoma
         (6) Hürthle cell tumor
      (b) Secondary carcinoma
         (1) Metastases from other organs (rare)
      (c) Sarcoma
         (1) Fibrosarcoma
         (2) Endothelial sarcoma
         (3) Lymphosarcoma
         (4) Osteosarcoma
         (5) Osteochondrosarcoma
      (d) Melanoblastoma
      (e) Hodgkin's disease
      (f) Teratoma

Simple colloid goiter may result from a previous hypertrophy and hyperplasia; that is, after the great demand is over, the gland may store thyroxin in *colloid* (thyroglobulin) for future use. There is an endemic type of colloid goiter caused by a deficiency of iodine in the water of

certain regions, such as Switzerland, and certain districts of the United States, as the Ohio Valley. Apparently iodine is needed for the synthesis of thyroxine and colloid is needed to store thyroxin. Therefore, in the nontoxic types there is always ample colloid. Since the colloid state is a resting stage in thyroid activity, the administration of iodine sufficient for the gland's requirements causes it to form an ample amount of thyroxin. This is then *stored in colloid for future use. In diffuse* colloid goiter which is untreated, the gland may be so large as to interfere with swallowing and even breathing, although the latter is rare and only occurs when there is great pressure on the trachea or when it has been dislocated by a unilateral enlargement. Interference with vocal cord movement (recurrent laryngeal nerve paralysis) usually implies that a malignant invasive growth is present with the colloid goiter.

Fig. 390.—Large colloid goiter involving chiefly the right lobe. Blood cholesterol, 227 mg.; basal metabolic rate, −25. Removal is indicated because of interference with breathing and swallowing.

Pressure on the acinar cells coupled with insufficient amounts of iodine are apt to produce a hypothyroid state.

The thyroid is the only organ in the human body which requires iodine; apparently no other gland uses it to elaborate a hormone, although it is found in many glands, especially in the pituitary.

The treatment for simple goiter is first its prevention. This may be easily accomplished by administering iodine by mouth during the "stress" periods. This prevents not only colloid goiter, but other types as well. One grain (.065 Gm.) of iodine (marine) per week is usually given during adolescence. The iodine does not eliminate a colloid goiter after it has formed; it does *prevent* it by keeping the gland in a normal

state of activity. The amount of iodine required by the body for thyroid activity is less than 1/1000 of an ounce. Iodine is best administered as iodized salt which will provide for adequate amounts when used for ordinary seasoning of food. If there is associated hypothyroidism, thyroid extract should be given. This medication is useful not only in the prevention of colloid goiter, but also in its treatment when seen early. If the gland is unusually large, unsightly, or interferes with respiration or deglutition, it is subtotally removed (subtotal thyroidectomy). The remaining gland will often return to a normal state if iodine is continued.

Adenomatous goiter is a benign growth of glandular tissue. It may be diffuse, without definite demarcations (diffuse adenosis), or of the so-called fetal type, which is an ingrowth of glandular tissue in a colloid-filled acinus, which looks as though it had a capsule. These areas are probably the involuted forms of previous hyperplasias. True adenomas sometimes occur. In addition to the changes noted, cysts may form due to retention caused by stroma bands or by necrosis due to pressure. Often calcification is observed, making the gland extremely hard. This hardness is observed in chronic thyroiditis and malignancy of the thyroid. However, calcification and malignancy in the same gland are extremely rare. Sometimes the entire gland is necrotic and the gelatinous cystic and hemorrhagic material may be scooped out at operation, leaving only the capsule with its blood vessels.

Embryonal adenomas (undifferentiated fetal adenomas) consist of solid nests or columns of epithelial cells with no acinus formation. This picture is very difficult to distinguish from carcinoma. *Fetal adenoma* (microfollicular adenoma) consists of many small acini containing little colloid and lined with cuboidal cells. The interacinar tissue often is sparse; however, at times, it may be plentiful, resembling hyaline tissue or colloid. The latter picture may resemble an ingrowth of epithelium into a distended colloid-filled acinus. *Colloid adenomas* are common and consist of acini of various sizes filled with colloid. *Papilary adenoma* or *papillary cystadenomas* are full of large acini with papillary projections of tall cuboidal or columnar epithelium resembling papillary cystadenomas in other glandular organs.

Clinically, adenomas are seen ten times more often in women than in men. They are rarely seen in children, occurring mostly after 30 years of age. The only symptoms and signs are those of a nodular swelling in the neck.

Complications include: (1) Carcinoma which is said to occur in 9 per cent of single adenomas and 4 per cent in multinodular goiters. (2) Toxicity which increases with the older age group. (3) Mechanical disturbances by compression and deviation of the trachea and esophagus by retrotracheal, substernal, and intrathoracic extension.

Statistics seem to indicate that carcinoma is more apt to occur in the nontoxic than the toxic nodular goiter. In addition, there are hypothetical grounds for believing that the rule of malignancy concerning in-

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Toxic Goiter (Thyrotoxicosis, Hyperthyroidism).—In addition to enlargement of the thyroid, the gland secretes something that makes the patient ill. Thyrotoxicosis is often referred to as hyperthyroidism; there is perhaps not only hyperthyroidism, but also a perverted secretion (a dysthyroidism). The word thyrotoxicosis implies that a toxemia exists, although no toxic substance has ever been identified. There is a low iodine content in the gland and an increase in blood iodine, but neither of these factors alone or in combination necessarily produce toxic goiter. For example, blood iodine may be elevated in cholecystitis with cholelithiases, essential hypertension, hypertensive cardiac disease, and certain infectious disorders, whereas a low thyroid iodine is seen in colloid goiter. The local changes in the gland are not always the same. Two principal varieties exist: (1) diffuse hyperplasia; (2) variable types of adenoma. The appearance of the gland grossly or microscopically does not indicate its toxicity.

Fig. 393.—Photomicrograph of tissue from a so-called fetal adenoma of the thyroid gland (medium power). This tissue was completely surrounded by a fibrous capsule, a portion of which is shown in the left lower corner. Note the small acini, the great vascularity, and the small amount of colloid. The appearance is that of fetal thyroid tissue.

Graves' disease or *Basedow's disease* is also called *exophthalmic goiter* because, in addition to other symptoms and signs, there is often a protrusion of the eyeball. Microscopically, the picture is one of diffuse hyperplasia. The cause is not known, although there is presumably an overstimulation of the thyroid by the pituitary through the thyrotropic factor of the anterior lobe. The disease is not hereditary but there is a strong familial tendency. Thyrotoxicosis may be induced by the ingestion of thyroid extract (factitial thyrotoxicosis, alimentary thyrotoxicosis). In endogenous thyrotoxicosis, the urinary excretion of radioactive iodine is low compared with euthyroid persons, but it is high in factitial thyro-

active glands holds in the case of the thyroid. If this is true, thiouracil should not be given in a toxic nodular goiter unless as a preoperative measure.

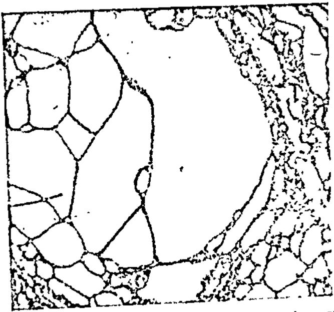

Fig. 391.—Section from a nodular colloid goiter. The section shows one of the nodules in which the acini are distended with colloid. The epithelium is of the low cuboidal type. There were no toxic symptoms.

Fig. 392.—Large adenomatous goiter in a woman aged 74. Pressure symptoms demanded operative removal. This was successfully accomplished.

The treatment for nodular goiter is thyroidectomy whether it produces symptoms or not because of the complications which may ensue, particularly carcinoma. After subtotal thyroidectomy has been done, biopsies should be done, and if carcinoma is found or suspected, total thyroidectomy with excision of lymph nodes is indicated.

Associated Clinical and Pathological Changes in Toxic Goiter.—Almost every organ and tissue in the body is affected more or less in thyrotoxicosis. The more common associated effects are in the brain, eyes, heart and blood vessels, liver, gastrointestinal tract, skeletal system (muscle and bone), endocrine glands, acid-base balance, carbohydrate and protein balance, and basal metabolism.

The psychoses may be due to cerebral edema such as occurs in burn toxemia or the toxemia of pregnancy. Small areas of necrosis may occur. The edema, the cardiac hypertrophy, the high pulse pressure, poor tolerance to hypoxia have been explained by some observers on the hypothesis that the hyperplastic vascular thyroid acts as an arteriovenous fistula. Indeed, they aver that the postthyroidectomy psychosis is due to increased edema because collaterals have not formed around the ligated thyroid vessels and adjustments have not occurred; the same reason is given for postthyroidectomy increase in exophthalmos; also the improvement in cardiac hypertrophy and the return to normal pulse pressure is said to be due to removal of the parasitic circulation (see Chapter 17).

Exophthalmos has been discussed previously under the discussion on Physiology of the Thyroid. The *heart* is often the seat of hypertrophy, and occasionally there may be small areas of necrosis or scars from previous areas or both. The *liver* may contain areas of fibrosis or necrosis as seen in severe burns or toxemia of pregnancy. Acute and chronic hepatitis and altered hepatic function are observed and may be discovered by liver function tests as previously described. These observations have led to the use of a high carbohydrate-protein and low fat diet with liberal amounts of vitamin B complex. There is a striking resemblance between some of the clinical features of hyperthyroidism and thiamine deficiency (tachycardia, cardiac hypertrophy, dyspnea, palpitation, edema, fatigue, lowered muscular strength, etc.). Hyperthyroidism increases the rate of cell metabolism, thus calling forth a higher requirement for food and an increase in the breakdown and resynthesis of metabolites. Thiamine is important in the latter processes. Pyruvic acid is an important intermediary in carbohydrate breakdown, and perhaps in the interconversion of protein, fat, and carbohydrate, and it is elevated in thyrotoxicosis. When there is an increased cellular metabolism, there will be a need for more thiamine and a relative deficiency in this vitamin. A high vitamin B diet delays the appearance of liver damage in thyroxine-treated dogs and decreases the level of pyruvic acid. Therefore, vitamin B complex is useful in the utilization of pyruvic acid, and this in turn makes for more complete breakdown and utilization of carbohydrates and protein which are needed to prevent further liver damage. There is good experimental evidence to show that hepatic injury is much more apt to occur in hyperthyroid animals who are anoxic than in hyperthyroid controls. The low serum proteins sometimes found may be due to the excessive utilization and breakdown of protein with increased nitrogen excretion, the fact

toxicosis. The cause is unknown, since the causative substance in the blood that is responsible has never been identified. Some of the contributory causes are understood; namely, the constitutional type, emotional stress, and autonomic imbalance. Sympatheticotonic symptoms are the tachycardia, exophthalmos, increased metabolism, fever, perspiration, and lessened gastric secretion. Increased peristalsis is vagotonic. The rapid pulse is thought by some to be due to a shunt across the greatly dilated capillary bed in the thyroid, which is comparable to an arteriovenous fistula.

Fig. 394.—Exophthalmic goiter in a girl aged 11 years. There were severe thyrotoxic symptoms, a basal metabolic rate of +35, and a blood cholesterol of 92 mg. Thyroidectomy was performed and was followed by an amelioration of symptoms. The gland showed diffuse hyperplasia. The exophthalmos is not pronounced.

Pathology.—The gland is enlarged, smooth, and beefy red (symmetric toxic goiter). The cells have enlarged and multiplied until the acini are full of tall cells with practically no colloid. The gland is red because its blood supply is greatly increased. Apparently the body takes away the thyroid secretion faster than the gland can produce it. The thyroid in primary thyrotoxicosis is poor in iodine and colloid. It has lost its power of retaining thyroxine in the colloid and discharges it in excess into the circulation.

The size of the thyroid or its microscopic picture is not in any way indicative of the presence or degree of thyrotoxicosis. There is no evidence that the cells produce an abnormal secretion.

Thyroid extract may produce a remission by relieving the gland of some of its work, thereby allowing capillaries to constrict and impeding the mechanism for the discharge of thyroxin. Once iodine is retained, a remission may occur. Blood from a thyrotoxic patient will cause tadpoles to metamorphose, but so will iodine.

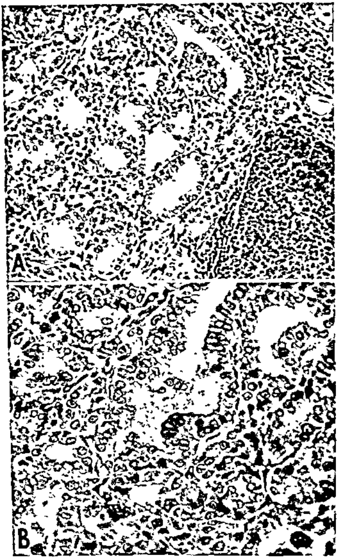

Fig. 396.—Tissue from an exophthalmic goiter. *A*. Medium power. Note the infolding of the epithelium into the acini, which are not large and contain very little lightly stained colloid. The lymphoid tissue in the right lower corner is a characteristic finding. *B* High power. The columnar cells are clearly shown, as is also their infolding in o the acini. This patient received iodine for a long period of time without remission of symptoms. Thyroidectomy was successfully accomplished in stages.

Symptoms and Signs.—Clinically, the disease is usually seen in young women who have had an unusual period of stress. It seems to occur in those with a "constitutional thyroid tendency," usually in individuals of the linear rather than the lateral type. There are heat intolerance and loss of weight in spite of enormous appetite. The patient

that there is impaired liver function interfering with the synthesis of serum albumin and fibrinogen, and the usual diet of thyrotoxic patients which is notoriously poor in protein. This combination of decreased intake, increased loss, and deficient synthesis is a vicious circle because hypoproteinemia causes liver impairment and vice versa.

The gastrointestinal tract exhibits changes in thyrotoxicosis which are more or less characteristic. These are (1) achlorhydria, (2) delay in gastric emptying, (3) increased small and large intestine tone and motility.

Fig. 395.—Exophthalmic goiter in a woman aged 28 years. The goiter is rather large and smooth. The exophthalmos is very pronounced. The anxious expression is typical.

Skeletal muscle may be atrophic and *bone* may show demineralization, imperfect calcification, or osteomalacia. There is an increased loss of calcium in the urine. Spontaneous fractures have been reported. The cortical portion of the *thymus*, the *pituitary*, the *spleen*, and *lymph nodes* shown hypertrophy. Disturbances in acid base balance may result in acidosis due to ketosis which is promptly relieved when liver glycogen is restored to normal. The profuse sweating, diarrhea, and vomiting are apt to cause dehydration with loss of electrolytes, especially in thyroid crisis.

Basal metabolism is greatly increased and the rate is high, plus 70 to 90 or more. Whole-blood *iodine* is elevated to about twice the normal (8 micrograms per 100 c.c.). The protein-bound (acetone-insoluble) blood iodine is presumably thyroglobulin in nature and is increased in hyperthyroidism and is decreased after the administration of gastrogenic drugs. Curtis believes that the basal metabolic rate and the protein-bound iodine determination are useful in detecting early cases of hyperthyroidism, especially in nodular goiter. If the BMR exceeds +10 per cent and the iodine is 1.2 micrograms, hyperthyroidism is suspected.

Therefore, it is better to give iodine only preoperatively in this type of goiter. How iodine acts is unknown. Iodine seems to have an inhibiting action on the excessive discharge of thyroxin. This is manifested not only by a return to normal histological architecture (accumulation of colloid, flattening of epithelium) and an increase in total iodine, but chiefly by an increase in the thyroxine iodine in the thyroid. Thus it seems that iodine does not exert its influence peripherally in the tissues but through the thyroid. Since the anterior pituitary shows relatively large amounts of iodine, this may also exert an inhibiting action by checking the production and secretion of the thyrotropic hormone. (Elmer.)

Fig. 397.—Toxic adenoma (nodular goiter) in a woman aged 69 years. This is the so-called exhaustion type of thyrotoxicosis, with emaciation, general weakness, loss of muscle tone, anorexia, and cardiac decompensation.

Some believe iodine acts on the thyroid by encouraging the formation of colloid, which decreases the activity of the gland by pressure. It may be that its good effect comes from the edema that iodine is known to produce in the capillaries or in the intima of the arterioles. This is especially true in new capillaries or young cells anywhere. This decreases

complains of palpitation, shortness of breath, and muscular weakness. The pulse is rapid and bounding. There are a high systolic and low diastolic pressure (large pulse pressure). Often there is exophthalmos, with lid lagging (von Graefe), or widened palpebral fissure (Stellwag). The enlarged gland is smooth and even. There are emotional instability, nervousness, tremors, and inability to sleep. There may even result what is known as a crisis (acute thyrotoxicosis); nausea, vomiting, diarrhea, and high fever, with delirium or coma.

The "thyroid storm" is a part of the disease and may occur not as a complication but during the course of thyrotoxicosis. It is a sudden exaggeration of all of the morbid and perverted functions of the central nervous, cardiovascular, and hepatorenal systems, and it may result in death from pulmonary or cardiac complications. It is seen in severe thyrotoxic patients and is apt to be initiated by (1) infections such as pneumonia or postoperative wound infection; (2) anoxemia from any cause whether anoxic (injury to recurrent laryngeal nerve, postoperative edema of trachea or its partial collapse, hemorrhage with pressure on the trachea), anemia from severe hemorrhage, stagnant from dehydration; (3) postoperative exacerbation; (4) following prolonged x-ray therapy without preparation; (5) hemorrhage and the necessity for secondary suture. It is more often seen in those patients who do not respond well to preoperative preparation. Acute thyrotoxicosis, or a crisis, may occur after thyroidectomy or after other operations if a goiter is present. Therefore, operation to remove the goiter usually takes precedence.

Exophthalmic goiter in children (juvenile exophthalmic goiter) is a familiar disease. It manifests itself as in adults but is much more severe. However, it is often overlooked because it is apt to occur during the adolescent period of childhood and the symptoms are attributed to physiological adjustments.

Treatment.—The disease goes through cycles of remissions and exacerbations, and in the treatment an attempt is made to produce a remission. Lugol's solution or iodine in any form, even by inhalation, is given for ten days. This and rest should produce an amelioration of symptoms, though it does not produce a permanent remission or cure. This may usualy be accomplished by the surgical removal of four-fifths or more of the gland.

Thus the treatment of thyrotoxicosis associated with diffuse hyperplasia resolves itself into producing a remission which is permanent. To achieve this, three lines of treatment have been pursued: (1) medical, (2) irradiation, (3) surgical. Usually a combination of medical preparation followed by adequate surgery is the surest method of producing a permanent amelioration of the disease.

MEDICAL TREATMENT.—

a. Iodine does not make a goiter nontoxic but does produce a remission long enough for the surgeon to perform an operation. If given over a long period of time, its ability to produce a remission is decreased.

in (1) those patients who refuse surgery, (2) those patients who have had surgery with recurrence but without a discernible goiter, or who cannot tolerate further surgery, (3) severe thyrocardiacs, (4) patients in whom a satisfactory remission cannot be obtained with the drug, with Lugol's solution, or x-ray therapy, (5) perhaps those in whom malignant exophthalmos is feared, although there is a difference of opinion concerning thyroidectomy in such cases; (6) the adolescent age group which may be tried on small doses because of the frequency of recurrence after thyroidectomy and the problem of deciding how much thyroid to remove; they must be carefully watched; (7) severe mental cases.

Thiouracil and its allied products are contraindicated (a) in those who are hypersensitive to the drugs, (b) in blood dyscrasias of all kinds, (c) in infections where granulocytes are needed, (d) in severe, long-standing exophthalmos, (e) over long periods of time in adolescence, (f) in toxic nodular goiter because of the danger of cancer, (g) in severe liver, kidney, or adrenal disease, (h) in pregnancy, (i) in large cervical, retrosternal, retrovasal, or retrovisceral goiter because increase in size may produce pressure symptoms and make surgery more difficult.

c. Radioactive iodine may be used in severe hyperthyroidism because the radioactive material goes to the most actively proliferating and hyperplastic cells, resulting in their necroses and replacement with fibrous tissue. Reports indicate that there are few side effects when doses ranging from 50 to 60 mc. are employed. The results are encouraging.

d. Irradiation of the thyroid gland may induce a remission by causing a decrease in blood supply and subsequent fibrosis. This is variable and unpredictable but useful in those patients who will not submit to thyroidectomy or in whom surgery is inadvisable or has been ineffective. Before x-ray treatment is given, patients should be prepared as for thyroidectomy, and if surgery is to follow, the surgeon must expect to encounter many adhesions between the gland and its capsule.

e. Irradiation of the pituitary gland to depress the secretion of thyrotropin has been suggested. The poor results and the danger of injury which might interfere with other functions of the pituitary have limited its use.

f. Miscellaneous medical treatment includes those measures which will improve the patient's general condition and help bring about a remission. (1) the diet should be high in calories. We have kept a caloric requirement curve in our thyrotoxin patients; as a remissoin occurs, the caloric needs and desires fall preceptibly, in severe cases, from 8,000 to 10,000 calories to 2,000 calories per day. Vitamins must be supplied, especially B complex, D, and C. (2) The administration of calcium and phosphorus in small doses is indicated. (3) Digitalis should be administered where necessary. (4) Quinidine should be given in fibrillation.

the blood supply and cuts down activity of the thyroid by retaining the iodine in the thyroid gland and preventing its excessive and perhaps premature loss into the blood stream. Iodine does not neutralize anything in the blood.

If iodine and thyroid extract are administered at the same time to experimental animals and man, hyperthyroid symptoms occur just the same. The chemical effects of iodine are well known. Tryptic ferments are present in the tissues and are normally inhibited by the unsaturated fatty acids. These may be converted into saturated fatty acids, thereby releasing tryptic ferments for autolytic action. The histologic effects of iodine are not well known. Diseased tissues or very young cells take up more iodine than normal adult tissues. The cells become swollen.

b. Thiouracil, Thiobarbital, and propylthiouracil decrease the synthesis of thyroid hormone within the gland. The amount of iodine within the gland and the blood is greatly decreased. The thyroid is enlarged and more vascular. However, the histological picture remains about the same; that is, there is the high columnar type of cell, with infolding in the acini, which contain very little colloid. Apparently these changes remain in the face of a decrease in the metabolic rate and abolition of the symptoms of hyperthyroidism due to the continuation of an excess of thyrotropic hormone. Thiouracil is given in 0.6 to 0.8 Gm. doses daily for about two weeks; then it is decreased. Thiobarbital is said to have ten times the antithyroid effect of thiouracil and is therefore given in much smaller daily doses, 50 to 60 mg. Propyl thiouracil may be administered in daily amounts of 200 to 300 mg. It is the least toxic of this group. However, in all there must be careful daily supervision lest severe side reactions occur, particularly granulopenia. Although some observers prefer to treat primary hyperthyroidism with these drugs, our observations have led us to employ them for preoperative preparation only, except in such cases in which surgery is contraindicated because of severe cardiac failure, mental derangement, or other causes. The reason for this is the great number of recurrences following the medical treatment described above. Since preparation with these drugs is accompanied by thyroid enlargement and an increase in vascularity, we discontinue the drugs after remission is apparent and then give Lugol's solution for eight to ten days to cause a recession in the size and vascularity of the gland, thereby making surgery easier. In some cases both drugs are used for a two-week period prior surgery, but even here we use iodine alone during the final preparatory period, with sulfadiazine for twenty-four to forty-eight hours prior to operation, particularly in extreme thyrotoxicosis.

Propyl thiouracil is not advocated as a routine preparatory measure, being used chiefly in extreme cases of thyrotoxicosis, or in thyrocardiac cases, or in those patients who do not tolerate iodine and who require a long period of preparation. The drug is used for prolonged treatment

in (1) those patients who refuse surgery, (2) those patients who have had surgery with recurrence but without a discernible goiter, or who cannot tolerate further surgery, (3) severe thyrocardiacs, (4) patients in whom a satisfactory remission cannot be obtained with the drug, with Lugol's solution, or x-ray therapy, (5) perhaps those in whom malignant exophthalmos is feared, although there is a difference of opinion concerning thyroidectomy in such cases; (6) the adolescent age group which may be tried on small doses because of the frequency of recurrence after thyroidectomy and the problem of deciding how much thyroid to remove; they must be carefully watched; (7) severe mental cases.

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(5) Thyrotoxicosis and diabetes produce a "symbiotic" picture because the thyroid speeds metabolism, demanding fuel, while the diabetes prevents proper utilization of glucose. Both diseases cause the patient to demand more and more food while he continues to lose weight rapidly. Therefore, insulin must be given along with propyl thiouracil and iodine. (6) Thyrotoxicosis and tuberculosis are a not uncommon combination; both diseases cause loss of weight and weakness. Iodine is not contraindicated in the preparation of the patient for surgery, which should be done as soon as feasible. (7) Children require special consideration. Surgery is deferred if possible because of the strong probability that a recurrence will take place. Furthermore, the surgeon does not like to remove too much gland since severe upsets in endocrine balance may ensue. This in itself ensures recurrence because the regenerative qualities of glandular tissue and especially the thyroid are greater in children than adults. If a remission can be maintained by propyl thiouracil, this should be done. If not, thyroidectomy which is less radical than for adults, is indicated.

SURGERY.—The treatment of choice in the great majority of cases is *thyroidectomy*. Two facts must be emphasized concerning thyroidectomy:

1. Thyroidectomy does not remove the cause of exophthalmic goiter, because it is not known definitely that the enlarged and hyperplastic thyroid gland is the determinant of the syndrome. It takes a link out of the chain of events. It is the best procedure to produce a permanent remission of symptoms, although it rests on an empirical basis.

2. Surgery is more apt to produce a permanent remission than any other method of treatment, although nature may accomplish this by atrophy (burning out of the disease). This is dangerous because heart, liver, brain, and other complications may occur during the waiting period, although some believe that organic heart disease is not caused by thyrotoxicosis.

Thyroidectomy should be performed after *adequate preparation.* Iodine does not always produce a remission. Remission is recognized by (1) the stabilization of the pulse, (2) the fall in the basal metabolic rate, (3) the stabilization of all emotional symptoms, (4) the gain in weight and strength. Other important circumstances which minimize the surgical risks are: the patient must have been given iodine for at least ten days, no fever or intercurrent infection must be present, the heart must be in compensation. Sometimes operations must be done in stages to avoid a "crisis." The first operation may consist of tying the superior thyroid arteries to produce a remission; then one or both lobes may be removed at the next procedure. This is not necessary as a rule.

Technique for Thyroidectomy:

This is done by making a "collar" incision in the neck, separating the "ribbon" muscles, and dissecting each lobe out of its capsule. The blood vessels are clamped and divided and the gland is partially removed, leaving the portion which lies next to the

trachea and esophagus (where the recurrent layngeal nerve lies) and the posterior part (where the parathyroids are situated). In toxic goiter almost the entire gland is removed. (See Fig. 398.)

Varations in technique: (1) Two-stage operations are done in very large goiters, doing one side at a time, because of the dangers inherent in removiing great pressure suddenly, with the consequent readjustments of organs and edema and interference with function as a result of these effects. Thus interference with breathing when both sides are removed is not only due to tracheal collapse but also to the enormous edema that comes from release of pressure. Thrombosis and embolism is also more apt to occur. (2) Two-stage operations in toxic goiter are now much less commonly done because remission can usually be produced by drugs. (3) Dissections may be done by first dividing the isthmus, then ligating the vessels and dissecting laterally, or first ligating the vessels and removing the lobe medially, but in every instance the blood supply is controlled by individual tying of each vessel by transfixed ligatures. (4) Identification of the recurrent laryngeal nerves is necessary when there is great displacement of structures and is done routinely by some surgeons. (5) The parathyroids are identified instead of being pushed aside with the capsule. (6) The ribbon muscles are divided transversely instead of being separated in large goiters.

Postoperative Complications of Thyroidectomy: The more common postoperative complications which may occur are (1) nerve injuries, (2) hemorrhage, (3) infection, (4) crisis, (5) parathyroid insufficiency, (6) respiratory difficulty.

Injury to the recurrent laryngeal nerve on one side results in homolateral paralysis with the vocal cord fixed in the midline. This results in a temporary change of voice, but in the presence of edema it may cause respiratory difficulty. When both nerves are injured, there is early loss of voice and then fixation in the midline of both vocal cords. This usually demands tracheotomy. But if oxygen is given, this may not be necessary, especially when the paralysis is temporary and the result of edema rather than injury. Great relief for bilateral cord paralysis is afforded by widening the space between the two vocal cords. This is done by dislocation and fixation of one of the arytenoid cartilages (King).

Hemorrhage is prevented by careful hemostasis and individual ligation of all vessels by transfixed ligatures. It is easily detected postoperatively when it appears on the dressings but is frequently overlooked when it is trapped in the thyroid bed (especially when large glands have been removed) and is unnoticed until respiratory stridor appears. The treatment is immediate surgery with reopening of the wound, removal of clots, and then, under Pentothal sodium or other anesthesia, careful ligation of the bleeding vessel.

Infection occurs rarely and when it occurs, it is usually the result of excessive postoperative bleeding. When tracheotomy or secondary surgery is necessary, the complication is more apt to occur. Penicillin and, if necessary, streptomycin are given and the pus evacuated when localization occurs.

Crisis has been discussed previously. Its treatment consists of (1) supplying sufficient oxygen to satisfy the increased metabolism; it is more effective in controlling the nervousness than sedatives; (2) replac-

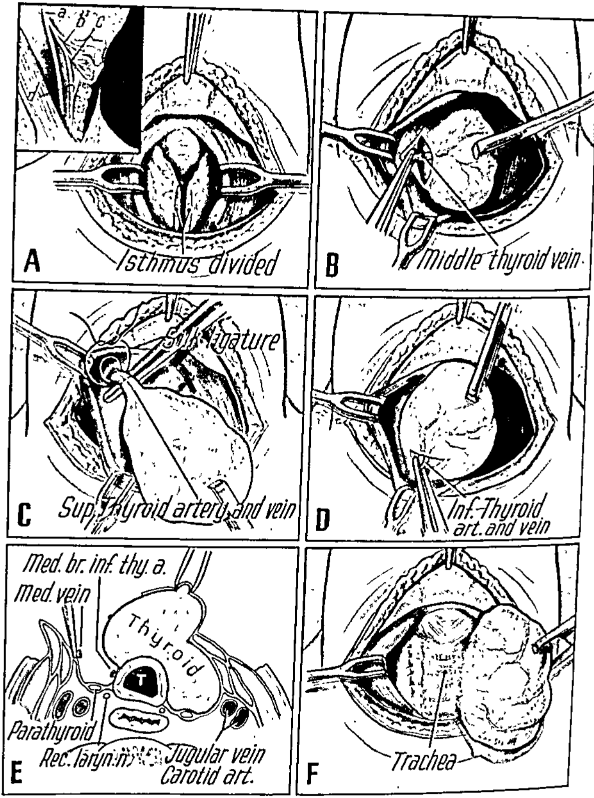

FIG. 398.—Thyroidectomy (subtotal).— *A.* A transverse incision has been made. The skin, subcutaneous tissue, and platysma have been divided. The ribbon muscles have been split longitudinally. The isthmus is divided between clamps, thereby converting the operation into two halves. Insert shows the related nerves: *a*, vagus, *b*, superior laryngeal nerve internal ramus), *c*, superior laryngeal nerve (external ramus); *d*, re-

(Continued on opposite page)

ing water and electrolytes which are lost by sweating, diarrhea, and vomiting; (3) supplying plasma and whole blood as indicated; (4) sulfadiazine and penicillin to combat infection, (5) glucose and vitamin B complex to protect the liver; (f) iodine and thiouracil should be continued. (g) Miscellaneous aids—lipocaic for the diarrhea, calcium gluconate to provide for the negative calcium balance, cold sponges for the excessively high fever.

Parathyroid insufficiency is rare and first manifests itself by numbness of the hands, general weakness, difficulty in focusing the eyes, and, later (after two to three days), carpopedal spasm. The blood calcium is lowered and inorganic phosphates raised. Treatment consists of large doses of calcium lactate orally or calcium gluconate intravenously. Dehydrotachysterol is given orally, 1 c.c. per day.

Respiratory difficulty may be caused by paralysis of the vocal cords, one or both, hemorrhage, infection, edema of the glottis, tracheal collapse, and tetany. If severe the condition may require tracheotomy before the cause is corrected in order to save life. All large goiters and substernal thyroids are removed under endotracheal anesthesia. At the conclusion of the operation the trachea is inspected with the bronchoscope and aspirated.

Sequelae to Thyroidectomy:

1. Hypothyroidism with or without myxedema occurs in a small group of patients. This late result may be treated with thyroid extract.

2. Recurrences are bound to occur since thyroidectomy is an operation which removes one of the manifestations of the disease and probably not its primary cause. The reasons for recurrence are (a) insufficient removal of the gland, (b) long duration of the disease before surgery, (c) persistence of social and economic problems, nervous shock. The treatment of recurrence is the treatment of the primary condition. However, propyl thiouracil with iodine may completely control the symptoms. X-ray treatment is occasionally effective. Operation may be necessary.

3. Persistent and progressive exophthalmus. This has been discussed under Physiology of the Thyroid. The thyroid-stimulating hormone is known to be an important factor in the formation of edema, including retrobulbar edema. Thyroxin is its antagonist, possessing de-

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current laryngeal. *B.* The middle thyroid vein is identified, clamped, and dissected loose from the lateral aspect of the thyroid gland and tied with a silk ligature. *C.* The superior pole is identified and the superior thyroid artery and vein are doubly ligated with transfixed ligatures. *D.* The inferior pole is freed and the inferior thyroid artery and vein are divided and ligated Care is taken to preserve the parathyroid glands. *E.* Transverse section showing the thyroid removed from its bed and the recurrent laryngeal nerves, parathyroid glands, and other important structures in the neck. *F.* The completed operation on one side The lobe is out and the remaining thyroid tissue, if any is left, is reconstructed by interrupted chromic 00 catgut sutures. The process is then repeated on the opposite side and the ribbon muscles are closed with interrupted sutures and the skin is also closed with interrupted silk sutures Usually, one drain is left in place for twenty-four to forty-eight hours to take care of any exudate or transudate that might accumulate beneath the ribbon muscles.

Carcinoma of the thyroid if limited to one lobe requires total lobectomy and radical neck dissection as shown in Fig. 136 if diffuse total thyroidectomy must be done.

hydrating and diuretic properties. Yet the administration *of thyroxin to relieve the exophthalmus is not often successful. Recently the adreno-corticotropic hormone has been tried with promising results.*

Toxic adenoma, or so-called **nodular goiter,** occurs in older people. These adenomas are the "tombstones" of a previous hyperplasia; perhaps the disease started earlier in life as a diffuse hyperplasia and then involutional changes occurred, producing a diffuse adenomatous goiter with some reactivated areas of hypertrophy and hyperplasia. The process is probably as follows: hypertrophy and hyperplasia; involution, with fibrosis, making more *divisions of the acini into groups resembling adenomas (as in adenosis of the breasts in involution). Some believe that thyrotoxicosis* in such glands is due to hyperplasia and hypertrophy of "unaffected" portions of parenchyma. As a rule, both pictures are present: hyperplasia and so-called adenosis. There is no evidence that the cells of an adenoma produce an abnormal secretion. They do appear to be autonomous, producing a small amount of thyroxin and dicodotyrosine, and, therefore, should be removed along with the rest of functioning gland. Carcinoma occurs more frequently in the single adenoma (about 9 per cent) than in multinodular goiters (about 4 per cent). The symptoms are not as severe as in exophthalmic goiter. It is not seen *often in young people. Frequently it occurs after the menopause.* The *treatment is the same. Rest in bed, propyl thiouracil,* and iodine usually *bring about a remission; then thyroidectomy is done.* Long-continued use of propyl thiouracil is contraindicated *because of the threat* of malignancy.

INFECTIONS OF THE THYROID GLAND

Infection in the thyroid gland is known as *thyroiditis.* It may be *acute or chronic. The acute varieties are caused* by the streptococcus, *staphylococcus, pneumococcus, typhoid bacillus, and* paratyphoid bacillus. Usually the infection *reaches the gland by the* blood stream (pneumonia, typhoid fever, puerperal *sepsis, influenza) but may* occur after injuries or by contiguity or by the lymphatics (*pharyngitis,* tonsillitis, Ludwig's angina). The symptoms are those *of an acute* inflammation with pain, swelling, tenderness, and even redness *of the skin;* there are chills, fever, leucocytosis, cough, dyspnea, and dysphagia *in the* more severe types. Complications are perforation of an abscess *into the* larynx or trachea, descent into the mediastinum with mediastinitis, pyemia. *The treatment consists of rest in* bed, penicillin and/or streptomycin, drainage of an abscess if this occurs. Late sequelae include hypothyroidism and myxedema.

Chronic thyroiditis may result from *specific* infections such as syphilis, tuberculosis, actinomycosis, trypanosomiasis (Chagas' disease) or it *may be nonspecific,* such as Riedel's struma (struma fibrosa, woody or *ligneous* thyroiditis), struma lymphomatosa (Hashimoto's lymphoid *struma),* giant-cell thyroiditis (pseudotuberculous of de Quervain).

Lastly, there may be amyloid deposits in the thyroid which result from chronic infections elsewhere. The specific varieties do not differ in their pathological appearances from the diseases elsewhere in the body. The nonspecific types are peculiar in their reactions. *Riedel's* struma is rare (about 0.3 per cent of all thyroidectomies). The gland becomes enlarged and very hard and is fixed to the capsule, which also becomes thickened. Microscopic examination discloses diffuse fibrosis in and around the lobules. Later, hyaline replaces much of the parenchyma. The acini becomes smaller, colloid decreases and becomes granular and watery, the epithelial cells are tall columnar with eosinophilic cystoplasm or cuboidal; some are degenerated. Giant cells, plasma cells, lymphocytes, and definite lymph follicle formation are seen. Clinically there is much pain with dyspnea, dysphagia, and some dysphonia. The patient is nervous and has a goiter, but the basal metabolic rate is normal. When limited to one lobe, the diagnosis between this condition and carcinoma is difficult and cannot be made without histological study. Treatment consists in bilateral subtotal thyroidectomy. This is done to establish the diagnosis and relieve constriction. The latter is served best when the isthmus is removed. Radical removal is not necessary and it is dangerous because the adhesions prevent careful protection of the parathyroids of recurrent laryngeal nerves. Since much of the functioning gland is destroyed, hypothyroidism and myxedema may follow thyroidectomy.

Struma lymphomatosa (Hashimoto's lymphoid struma) consists of an enlarged thyroid due to excessive amounts of lymphoid tissue. This frequently leads to decreased thyroid function and myxedema. The gland is smooth and enlarged and is hard. The lymphoid infiltration is either in the form of single cells or well-defined follicles with germinal centers. Most of the epithelial cells are low or tall cuboidal; some are larger with pale eosinophilic cytoplasm and are identical with Hürthle cells. There is not much increase in connective tissue, and the blood supply is normal. Clinically it is usually seen in women at or near the menopause. The thyroid is diffusely enlarged and causes *some pressure symptoms*. The patients usually complain of symptoms which are more or less typical of myxedema. The basal metabolic rate is often subnormal. Treatment is usually conservative thyroidectomy to relieve pressure symptoms and above all to establish the diagnosis.

Giant-cell thyroiditis (pseudotuberculosis, de Quervain's) has been accepted as an entity by some pathologists who say it does not evolve into any other type. Others have not been willing to call it tuberculosis, although the granulation tissue closely resembles the tubercle formation of this disease, because tubercle bacilli have not been found, preferring to classify it rather as a stage or stages in the evolution of any varieties of chronic nonspecific thyroiditis. In favor of the latter concept is the fact that the typical pictures as described in Riedel's and Hashimoto's struma are the end results. Almost any combination of reaction to in-

jury by the stroma or the epithelium may be *encountered in the early stages.* Clinically there are *pain, dysphagia, and low-grade fever. The thyroid is diffusely enlarged and very tender.* The patients are weak and *nervous with tachycardia,* but the basal metabolic rate is usually *normal.* The *diagnosis is suspected* in many cases, and the disease may be *successfully treated with x-rays.* However, most surgeons prefer *limited thyroidectomy* to be sure of the diagnosis as well as to relieve *symptoms.*

Tumors and Cysts

The thyroid acini rarely become cystic. Follicular cysts are due to hemorrhage into the follicles. They contain some colloid, degenerated blood, and often cholesterol. The wall is made of the follicle and gland capsule which also has new connective tissue. Adenomatous cysts are due to necrosis in the center of an adenoma with subsequent softening and hemorrhage with blood pigment which is absorbed later, leaving clear fluid which is yellow in color. The wall is made of the adenoma capsule and neighboring compressed gland. Calcification often occurs.

Benign tumors are chiefly epithelial but may be made of any of the gland's constituents. The more common varieties are adenoma, fibroma, endothelioma, and plasmacytoma. Of this group the adenomas are of prime importance. They vary greatly in their microscopic appearance and in their function as previously described in this chapter.

Malignant tumors may be primary or metastatic. Primary carcinoma is more common than was formerly thought, occurring in about 3 per cent of surgically removed goiters. About 35 per cent of carcinomas are said to arise in pre-existing adenomas or in situ. Furthermore, they are more apt to occur in the nontoxic varieties, or at least hyperthyroidism or thyrotoxicosis is found in only about 3 per cent of thyroid malignancies. Since thiouracil produces changes of a hyperplastic nature, and since it also decreases function, it should be used cautiously in toxic adenoma. As we have seen in Chapter 15, an anaplastic tumor retains less of the normal function of its constituent cells as the degree of anaplasia advances, although hyperthyroidism may be an adjunct of malignant neoplasia. Various types of carcinoma are seen. Those of low grade are the malignant adenoma (probably the so-called benign metastasizing goiter belongs in this group), papillary carcinoma, and Hürthle-cell carcinoma. The moderately malignant is the adenocarcinoma, whereas the highly malignant are the small-cell carcinoma and the giant-cell (and spindle-cell) carcinoma. The microscopic picture is extremely variable in its architecture and cell types as well as its size, which may be extremely small or very large. However, if the epithelial growth invades the capsule or blood stream, it is malignant regardless of its microscopic appearance, and perhaps the reverse is true for benign tumors. *Clinically* the lesions are insidious and occur at any age, even in children; usually, however, they occur between 45 and 70 years. The

growths are discovered in what is thought to be a benign adenoma, or, because of the age, recent rapid growth of the goiter, and its firmness, the lesion may be suspected and found localized in its capsule. The more highly malignant carcinomas may be associated with symptoms of hyperthyroidism. This is not often the case in lower grade carcinomas. The explanation for this is not clear.

Another group will show early involvement of the recurrent laryngeal nerve or trachea, indicating extension. Late cases show x-ray evidence of bone metastasis. These already have lymph node involvement and often the lungs as well. There observations clearly show the routes of spread by both blood and lymph channels. Indeed, many of the so-called lateral aberrant thyroid tumors are lymph nodes filled with carcinoma from the homolateral lobe. *Treatment* consists of radical excision (total) of the lobe involved, together with nodes, along the carotid sheath and superior mediastinum in the less malignant types, whereas in late cases or the more malignant varieties, total thyroidectomy and removal of nodes on both sides is indicated. In all cases, x-ray treatment is given postoperatively. Radioactive iodine is useful for diagnosis and treatment of bone and other metastases. The prognosis in the early and less malignant types is excellent. In the diffuse varieties or in those of the less anaplastic types which have spread or in the mixed types, the prognosis is poor. Frequently the lone lesion leads to the diagnosis. In such cases the bone metastasis and the primary growth must be removed. X-ray treatment should follow.

Secondary malignancies of the thyroid are rare; however, hypernephromas, malignant melanomas, and carcinomas from the lungs and gastrointestinal tract have been reported. The explanation for this infrequency of metastasis is conjectural. Two theories have been advanced: (a) the rich arterial supply inhibits the lodgment of emboli in the gland and (b) chemical factors such as the high oxygen and high iodine content may be inhibitory factors in contrast to the low oxygen content in the liver. Neoplastic cells need very little oxygen.

Other malignancies include sarcomas (fibrosarcoma, endothelial sarcoma, lymphosarcoma, osteosarcoma, osteochondrosarcoma), melanoblastoma, Hodgkin's disease, and teratoma. These tumors are not diagnosed preoperatively as a rule. Wide excision with subsequent x-ray therapy is the treatment. If one lobe is involved as is often the case, total lobectomy and radical neck dissection as described in Chapter 16 should be done. If there is wider involvement, total thyroidectomy is indicated with radical neck dissection.

Insufficient Thyroid

Sometimes myxedema (cachexia strumipriva or thyreopriva) is caused by removing too much of the thyroid gland. The causes of insufficient thyroid secretion are congenital absence of the thyroid, infec-

tion, atrophy, atrophy with nodules which are functionless or cystic, large colloid goiter (due to pressure on the functioning cells), and postoperative deficiency. Not all hypothyroid states produce myxedema, which is probably a late phase. Myxedematous patients are edematous and torpid but may still be "nervous." The edema is not a true collection of fluid in the skin and subcutaneous tissues unless there is associated cardiac damage. The deposit of a semifluid albuminous substance (like the white of an egg—13 per cent protein) in the skin resembles edema. A pure carbohydrate diet diminishes it and a diet rich in protein increases it. This is thought to be due to the great osmotic pull of the tissue fluid and an increased permeability of the capillaries. (See Chapter 6.) Clinically the skin is dry and scaly, the hair falls out, the voice is coarse, and physical and mental activities are depressed. The basal metabolic rate is low, and the blood cholesterol is high. There is anemia (macrocytic) and achlorhydria in many cases. The patient thus becomes a hibernating animal.

Other changes are as follows: (1) The blood (decrease in plasma volume, increase in plasma protein, decrease in water and chlorides, and increase in bicarbonate); (2) circulation (decrease in minute volume and prolongation of circulation time—the opposite of hyperthyroidism; myxedematous changes in heart muscle); (3) edema (increase in *intracellular* water; in cardiac edema the increase in *intercellular*); (4) cerebrospinal fluid (increase in protein concentration—the opposite from hyperthyroidism); (5) calcium (excretion diminished and bones more dense—the opposite from hyperthyroidism); (6) menses (usually but not always prolonged—the opposite from hyperthyroidism); the treatment is the administration of thyroid extract.

The Parathyroid Glands

The parathyroid glands (epithelial bodies, parathymic glands, branchiogenic glands) are yellowish brown spherelike structures measuring about 10 to 20 mm. in diameter. From the dorsal part of pharyngeal pouches III and IV come the parathyroids which at the 20 mm. stage are detached along with the thymic and ultimo branchial bodies. The pair from the third pouches is drawn down by the migrating thymus to the lower level of the thyroid gland. The pair from the fourth pouches does not shift much and becomes the upper parathyroids. The two upper glands are, therefore, distinguished by the number IV and the two lower by the number III. Parathyroid IV is usually embedded in the tunica propria of the thyroid and lies on its posterior side at about its middle (lower level of cricoid cartilage), whereas parathyroid III lies in a similar position at the inferior part of the thyroid. The best guide to them is the anastomosing channel connecting the inferior and superior thyroid arteries which give off branches (superior or inferior or the anastomosing channel) to supply the glands. The normal parathyroid gland weighs 30 to 40 mg. and measures 6 to 7 mm. by 3 to 4 mm. by 1 to 2 mm. Variations do occur. The largest glands will measure 15 by 6 by 3 mm. and weigh up to 100 mg. Usually four glands are present (80 per cent); sometimes there are six or more (6 per cent) and sometimes less than four (14 per cent). When more than four are present, the supernumerary glands are situated in the immediate vicinity of the normal glands. When less than four are present at operation, there is likelihood that they have been missed. The gland is soft,

oval, and smooth. Its surface appears finely granular due to minute vessels beneath the capsule which enter at the hilus. Before puberty the color is coffee brown (due to chief cells). After puberty fat appears and the color is more of a yellowish-brown. Sometimes the gland lies in a pod of fat.

Congenital Anomalies of the Parathyroid Glands.—Sometimes in the course of development, the parathyroid primordia divide into many parts, giving rise to eight to twelve glands. All segments from the third pouch are numbered III and those from the fourth are numbered IV. Parathyroid IV may be found behind the pharynx and esophagus, in the fibrous tissue at the side of the larynx above the level of the thyroid gland, on its anterior surface behind any part of the homolateral lobe of the thyroid gland, or embedded in the thyroid substance (internal parathyroid). Parathyroid III may be found near the bifurcation of the common carotid, the sides of the trachea, behind any part of the homolateral lobe in the superior mediastinum, or in the thorax.

The normal parathyroid is made up of chief or principal cells up to puberty, which probably give rise to the oxyphile cells and the water-clear cells (wasserhelle). The latter are in some normal glands after puberty, whereas oxyphile cells are found in increasing numbers with age.

Physiology.—The parathyroid hormone has a great influence on the metabolism of calcium and phosphorus. Practically all of the body's *calcium* is in the form of a calcium phosphate calcium carbonate compound which is found in the matrix of bone and teeth and in body fluids. In the blood it is mostly in the form of calcium ions and calcium proteinate. When the calcium ion is low, the parathyroids are stimulated and regulate the level of calcium ions. Calcium is lost chiefly in the urine and feces and, to a lesser extent, in the lactating breast and placenta. Deficits are made up by the mobilization of calcium from the bones and perhaps the teeth—excess amounts are stored in these structures. Serum calcium remains constant (10 to 12 mg. per 100 c.c.).

Phosphorus is also found in bones and teeth just like calcium in a ratio of about 2 to 1 and in small amounts in body fluids. In the serum phosphorus an inorganic phosphate is found in amounts of 3 to 5 mg. per 100 c.c. (lower in adults, higher in children). Organic phosphates (phosphoprotein, phospholipids, various phosphate esters) liberate phosphate ions on hydrolysis, though these do not necessarily reach the bones.

In the absence of parathyroid secretion there is a decrease in phosphorus excreted in the urine, an increase in serum phosphorus level, a decrease in serum calcium and its diminished excretion in the urine. When parathyroid extract is given to a normal person, the reverse of the above is true.

A reciprocal relationship exists in the blood between calcium and phosphorus concentrations. Phosphate retention or injection causes a fall in serum calcium; conversely a rise in the calcium of the serum tends to depress the inorganic phosphorus of the blood. If too much parathyroid extract is administered to the experimental animal, "parathyroid poisoning" may ensue, with calcium deposits in the alveoli of the lungs and mucous membranes of the stomach and the kidneys. The sequence of events is a high level of serum calcium, an acute failure of the kidneys to excrete phosphates with a rise in serum phosphorus, and, at the same time, a high serum calcium and high serum phosphorus, a precipitation of calcium phosphates into the tissues, and chemical death (Albright).

Functional Derangements of the Parathyroid Glands

Hypoparathyroidism usually occurs as a result of the inadvertent removal of the parathyroids during thyroidectomy or, more commonly, through interference with their blood supply. Sometimes the condition occurs idiopathically or even more rarely due to congenital absence of most of the parathyroid tissue. Hypoparathyroidism causes a fall in the

serum calcium from 10 to 12 mg. per cent (normal) to 7 or 8 mg. per cent and a rise in serum phosphorus from 5 mg. per cent (normal) to 6 to 8 mg. per cent. No calcium is secreted in the urine. Clinically the syndrome known as *tetany* is exhibited. The chief symptoms are neuromuscular excitability which is dependent on hypocalcemia. This irritability is manifested as carpopedal spasm, Chvostek's sign (tapping of facial nerve, causing facial muscle spasm), Trousseau's sign (obstructing circulation of arm by cuff, causing hand spasm—accoucheur's hand), Erb's sign, increased excitability of muscles to galvanic current, laryngeal spasm, epileptiform seizures in long-standing cases. Cataracts, brain calcification, and increased bone density have been described. In the acute state there is rapid breathing (which intensifies the clinical symptoms due to alkalosis), high fever, tachycardia, salivation, and fibrillary twitchings, and death may ensue.

Differential diagnosis. Tetany may be caused by a number of conditions other than parathyroid deprivation. The following is a list of some of the more common causes. In some cases, a combination of causes may be causal.

1. Calcium deficiency
   a. Diminished intake or insufficient amounts as in pregnancy; excessive loss as in lactation (milk fever of cows)
   b. Lack of adequate absorption (sprue, celiac disease, diarrhea)
   c. Metabolic deficiency; defective utilization and assimilation of calcium due to lack of vitamin D, as in rickets and osteomalacia, "laryngismus stridulus" and spasmophilia in general.
   d. Abnormal control due to parathyroid deficiency
   e. Renal insufficiency with phosphorus retention and compensatory lowering of serum calcium.
2. Alkalosis (calcium normal, phosphorus increased)
   a. Chloride deficit from vomiting or continuous gastric suction
   b. Excessive bicarbonate from ingestion of soda bicarbonate
   c. Carbonic acid deficit from hyperventilation may explain "freezing at the sticks" in aviation, "cramps" in cold water swimming
3. Miscellaneous causes (experimental)
   a. Magnesium deficiency
   b. Intravenous injection of alkaline phosphate (not acid phosphate)

The treatment of parathyroid tetany includes the administration of dehydrotachysterol (like vitamin D, it is a photochemical derivative of ergosterol), about 3 c.c. per day, until calcium appears in the urine; calcium and vitamin D; a diet rich in calcium and low in phosphorus. Parathyroid extract is available and effective for short periods.

Other types of tetany are treated by first correcting the cause and then giving calcium if there is a deficiency in the form of gluconate or lactate. Alkalosis tetany demands relief of hypochloremia, increased CO_2, or administration of acidifying salts such as ammonium chloride, depending on the cause (see Chapter 12).

Hyperparathyroidism may be primary (more parathyroid hormone produced than needed) or secondary (more parathyroid hormone than normal produced for compensatory purposes as in rickets, osteomalacia, and renal insufficiency). The *causes* of hyperparathyroidism are (1) neoplasms (adenoma usually and rarely carcinoma) and (2) hypertrophy and hyperplasia.

Adenomas may be present in one (usually) or more of the parathyroids. The lower glands are the seat of adenomas in about 80 per cent of the reported cases. In 10 per cent the parathyroids were in an abnormal portion (60 per cent of this group were in the mediastinum, 30 per cent in the substance of the thyroid, and 10 per cent behind the esophagus). The size varies from 10 to 3,500 times the normal, but the average will be about 3 by 2 by 2 cm., weighing about 7 grams. The only way the surgeon can distinguish between adenoma and hyperplasia grossly is by the fact that in the latter instance all glands will be uniformly enlarged. Histologically adenomas present a mixture of chief, water-clear, and oxyphilic cells together with transitions between these forms.

Hypertrophy and Hyperplasia.—In hypertrophy the amount of parathyroid tissue is greatly increased due to an enormous increase in the volume of the normal cell. In hyperplasia there is a uniform replacement of the normal gland with large-sized water-clear cells.

Abnormal Physiology.—The serum calcium is high (up to 18 mg.). Serum calcium exists in two forms: (1) nondiffusible, which is bound to serum protein (chiefly albumin) and constitutes about 45 per cent of the total serum calcium; that is, about 4-5 mg. per 100 c.c.; (2) diffusible, which exists in an ionized form and represents about 55 per cent of the serum calcium (5-7 mg. per 100 c.c.). Because of the large amount of nondiffusible calcium which is normally present, a serum protein determination should be done. If this is low, the total serum calcium may be normal, yet the calcium ions which are high in hyperparathyroidism would be greatly increased. Serum phosphorus is low (3 mg. or less unless renal damage is present). Calcium and phosphorus excreted in the urine are both increased. If the hyperparathyroidism leads to bone disease (which is not always the case if the patient gets enough calcium in his diet), the phosphatase level is increased (20 to 30 Bodansky units).

Symptoms and signs are usually of three general variieties: (a) those due to bone disease—*osteitis, fibrosa cystica generalisata,* (b) those due to renal disease; (c) those due to the hypercalcemia.

Bone disease is seen as an increased amount of absorption with an increase in the number of osteoclasts. Bones are easily injured, but the reparative powers are unimpaired and osteoblasts are plentiful. With the increase in osteoblastic activity, there is an increase in serum phosphatase which, in the absence of hepatic disease, is evidence of bone building. Bone matrix laid down around the osteoblasts is calcified, and

there is an increased amount of stroma in the bone marrow with fibrosis. Solid or semisolid tumors are sometimes seen which are made up of osteoblasts and osteoclasts; these are known as benign *giant-cell tumors* or osteoclastomas. In the jaw this kind of tumor is known as epulis. The bone cysts filed with fluid and lined by fibrous tissue are due to secondary degenerative changes and may be found anywhere in the body—generalized osteitis fibrosa cystica (von Recklinghausen's). (See Chapter 21.) Spontaneous fractures and vague pains in the back or legs are often the first manifestations of the disease. The bone disease must be differentiated from osteoporosis due to other causes such as: osteomalacia, osteitis deformans (Paget's disease), multiple myeloma, metastatic malignant neoplasms, osteitis fibrosa disseminata (polyostitic fibrous dysphasia), a regional disease with increased density and porosity occurring in young females, xanthomatosis, Gaucher's disease, lymphoma, hemangioendothelioma, osteogenesis imperfecta (osteopsathyrosis), chronic radium poisoning. The diagnosis is established by x-ray studies, biopsy, and blood and urine studies.

Rickets and *osteomalacia* are due to vitamin D deficiency and interference of absorption of calcium from the gastrointestinal tract. This causes a low serum calcium which in turn stimulates the parathyroids to increased activity with the production of more hormone which leads to a decrease in serum phosphorus. The glands hypertrophy to meet the demands. The final result is a normal serum calcium and a low phosphorus level. If the parathyroids do not hypertrophy, the calcium is low and the phosphorus normal; if both values are low, the glands have not kept pace with the hypocalcemia. This type of hyperparathyroidism is *secondary* and not primary

Renal disease is due chiefly to the excretion of increased amounts of calcium and phosphates in the urine with the formation of calcium phosphate or calcium oxalate *calculi*. Calcium salts may be deposited in the pyramids (nephrocalcinosis), leading to renal insufficiency. Polyuria and polydipsia are as common in hyperparathyroidism as in diabetes mellitus and insipidus.

Renal insufficiency may give rise to *secondary* hyperparathyroidism, "renal rickets," or may result from primary hyperthyroidism. In the former there is retention of nonprotein nitrogen and also retention of serum phosphorus with tendency toward low serum calcium and hyperplasia of the parathyroids to correct the low calcium level. In some cases it may be accompanied by osteitis fibrosa cystica, "renal osteitis fibrosa cystica"—Albright. The secondary hyperparathyroidism probably prevents tetany in these cases.

The renal damage resulting from parathyroid adenoma and hyperparathyroidism leads to phosphate retention and low calcium, and the body demands for parathyroid hormone may equal the increased amount secreted by the secreting adenoma. Thus in all types of hyperparathyroidism with renal insufficiency less parathyroid tissue is removed.

Hypercalcemia induces decreased neuromuscular excitability, decreased blood coagulation time, fall in inorganic phosphorus, and high plasma phosphatase increase in urinary calcium. Many diseases may be confused with hyperparathyroidism; namely, acute osteoporosis, hypervitaminosis D, sarcoidosis, myelomatosis, carcinomatosis with extensive bone involvement, polyostotic fibrous dysplasia, renal osteitis fibrosa generalisata, and osteomalacia. When associated with hypercalcemia and renal damage, differential diagnosis may be difficult. Hypercalcemia without hypercalciuria or decrease is serum alkaline phosphatase, and accompanied by calcinosis and renal insufficiency, may result from prolonged intake of milk and alkali.

The treatment for primary hyperparathyroidism is the removal of the adenoma or adenomas or in the secondary varieties the removal of some of the excessive parathyroid tissue. A few rules to follow in parathyroidectomy as follows: (1) A methodical search should be made beginning with the left superior, then the left inferior, the lower levels of the inferior thyroid veins, then the other side. (2) Biopsy is not taken until all parathyroid tissue has been inspected. (3) Normal parathyroid should not be removed because it will not help the condition and, if later on, adenoma is found and removed, tetany may occur. (4) If a parathyroid is not found in the normal position, further search is necessary in the region of the missing gland. If it is the superior, search is made from the lipoid bone to below the thyroid (all around the superior pole, between the thyroid and trachea, trachea and esophagus, behind the esophagus around the carotid). If the inferior is missing, one must *search the anterior superior mediastinum and posterior superior mediastinum* all along the inferior vessels. If there is none found and if the thyroid is nodular, a lobe of this gland may be removed in the hope that the parathyroid is embedded. (5) Anterior superior mediastinal exploration should not be done at the same time that the neck is explored. If the missing gland and adenoma have not been found, several weeks should elapse to see whether the patient is improved; then exploration should be done by splitting the sternum. Even thymectomy may be indicated. (6) Complete removal of the adenoma is indicated because of the possibility of carcinoma. (7) Sometimes postoperaive tetany ensues for a while. However, in the presence of hyperparathyroidism, the diet should be low in calcium lest "parathyroid poisoning" occur.

Primary carcinoma of the parathyroid is rare. It grows expansively and metastasizes to the regional nodes and lungs. It may or may not be endocrinologically active, usually not. The diagnosis is very difficult in the early stages and can only be established by biopsy. However, these glands are apt to be more firm, adherent, and invasive. Therefore, all parathyroid tumors should be widely removed, and if microscopic study shows any malignant change, lymph node biopsies should be taken. If metastases are present, a wide dissection of the involved side of the neck is indicated. X-ray treatment appears to be ineffectual.

The Adrenal Glands

The adrenal or suprarenal glands lie at the upper pole of the kidneys. The two glands together weigh about 10 to 12 grams. They are richly supplied with blood by the superior suprarenal artery (from the inferior phrenic branch of the aorta), the middle suprarenal (directly from the aorta), and the inferior suprarenal (from the renal artery). The capsule contains the arteries, a nerve plexus, and some collections of sympathetic ganglion cells and sends a fine network of reticular fibers into the cortex, along with the capillaries. The capillaries empty into anastomosing sinusoidal blood spaces, which in turn drain into the central veins, which unite and emerge as a single vein. This empties into the inferior vena cava (right) and the renal vein (left). The sinusoids in the cortex are lined with endothelial cells and macrophages. About twenty to thirty nerves enter each gland, most of them coming from the celiac sympathetic plexus, some from the greater splanchnics, and a few from the vagus.

The glands are divided into a cortex and medulla. The latter contains chromaffin and sympathetic ganglion cells. The cortex develops from the mesoderm of the Wolffian ridge; the medulla from ectoderm, which gives rise to the sympathetic ganglion cells.

The medulla elaborates adrenaline (epinephrine, adrenin, or suprarenin). The effects initate those of stimulation of the sympathetic nervous system and are, therefore, said to be sympathomimetic. The sympathetic fibers liberating an adrenaline-like substance (sympathin) are said to be adrenergic, that is, postganglionic fibers to the heart causing cardioacceleration and to blood vessels causing vasoconstriction, etc., as distinguished from those fibers of the parasympathetic and sympathetic (to sweat glands, vasodilators, and to adrenal medulla) which liberate acetylcholine and are called cholinergic (see Chapter 18). Some of the more important actions of adrenaline are: (1) Blood vessels are affected in different ways, depending on their location. Arterioles and capillaries of the skin, mucous membranes, splanchnic viscera (except the intestinal vessels) are constricted; the vessels of skeletal muscles, the coronaries, and the intestines are dilated. (2) The heart is slowed by adrenaline, but since this effect is produced through the carotid sinus and aortic nerves as a result of elevated blood pressure, it cannot occur where there is a great loss of blood volume. (3) Plain muscle is inhibited (stomach, intestine, bronchiole, wall of urinary bladder) so that intestinal movement is inhibited, bronchioles are dilated, and the urinary bladder does not contract, whereas the trigone and sphincter do sometimes, causing urinary retention. Muscles of the gall bladder, ureter, and pyloric, ileocolic, and anal sphincters are excited. Skeletal muscle shows a delay in fatigue. (4) Respirations are increased in rate and depth. (5) Carbohydrate metabolism is increased and hyperglycemia and glycosuria result due to mobilization of sugar from the liver, decreasing its glycogen as well as that of muscles. (6) General metabolism is also increased. The adrenal medulla is not essential to life. Dibenamine hydrochloride (dibenzyl beta-chloroethylamine hydrochloride) is an adrenolytic drug blocking the effects of adrenaline and is therefore useful in the diagnosis and treatment of diseases of the medulla producing excessive amounts of adrenaline, such as the pheochromocytomas. Any of the benzodioxan derivatives are useful as indicators of excess epinephrine since they lower the blood pressure due to this hormone but do not lower it in essential hypertension. The injection of .05 mg. histamine intravenously will precipitate a hypertension crisis in pheochromocytoma perhaps due to the vasodilation and increased amounts of adrenaline thrown into the circulation.

The emergency theory of epinephrine secretion holds that since it is secreted in greater amounts during nervous excitation, it is needed to make the body more efficient (in energy spending) during such crises (Cannon). The tonus theory assumes that the sympathetic nerve endings are being stimulated continuously, thus keeping up

the vascular tone and the blood pressure. Epinephrine is secreted in small quantities and is rapidly destroyed in the blood stream.

The cortex is necessary to life. If most of it is destroyed, as in Addison's disease, death follows unless prevented by replacement (cortin). Completely adrenalectomized animals have loss of appetite, vomiting, diarrhea, weight loss, weakness, low body temperature, and low basal metabolic rate. They may be maintained without any other medication for months if given large amounts of salt, that is, NaCl, or sodium citrate. Some observers believe that this is more important than the administration of cortin in Addison's disease. With the sodium ion decreasing in the blood because of its increased excretion through the kidneys, there is commonly also a drop in bicarbonate ion, as well as in the chloride ion. Because of this, Wilder and Allers have felt that a sodium salt without a fixed acid radical should be administered in addiiton to the sodium chloride. Therefore, sodium citrate or sodium bicarbonate is given with the sodium chloride. One-tenth of the gland is sufficient to maintain life in experimental animals. During adrenal insufficiency there is an increased excretion of sodium by the kidneys, and there are increased amounts of potassium and nonprotein nitrogen in the blood.

Crystalline compounds extracted from the cortex are oxygenated steroid derivatives. Of the identified steroids is one with the property of male sex hormone (dehydroisoandrosterone), a beta ketosteroid that is closely related to the male sex hormone androsterone, an alpha ketosteroid. Also female sex hormones are secreted—estrone and progesterone. Androgens and estrogens are found in the urine of small children of both sexes. In normal adults the estrogens decrease in males and the androgens decrease in females. Other steroids have effects on salt and water metabolism, permeability of the capillaries, regulation of carbohydrate, fat and protein metabolism, renal function, capacity of muscle response, and resistance to stress. Desoxycorticosterone is useful in deficiency states but has no demonstrable effect upon carbohydrate metabolism; that is, the hypoglycemia seen in cortical atrophy or destruction by granuloma or neoplasia.

Active compounds isolated from the adrenal cortex and their effects are listed in Table XXVII.

TABLE XXVII

(Slightly modified from Walters and Sprague: J. A. M. A., 1949.)

EFFECT	COMPOUND
Salt and water	Desoxycorticosterone
Carbohydrate, protein metabolism; antiarthritic?	17-hydroxy-11-dehydrocorticosterone (Compound E)
	11 dehydrocorticosterone (Compound B)
	17-hydroxycorticosterone (Compound F)
Fat metabolism	11 dehydrocorticosterone (Compound A)
	Corticosterone (Compound B)
Androgenic effect	Androstenedione
	11-hydroxy iso-androsterone
	17-hydroxyprogesterone
Estrogenic effect	Estrone
Progestational effect	Progesterone

The adrenal cortex is related to the sex glands and thyroid as well as the pituitary. The cortex hypertrophies during pregnancy. Hypertrophy of the cortex causes sexual precocity in children and virilism in girls. There is a very close relationship between the thyroid and the adrenals. Hypophysectomy causes atrophy of the cortex, and injection of hypophyseal extracts causes an increase in the mitoses in the glomerular and outer fascicular zones. The cortex is rich in ascorbic acid (vitamin C).

Higgins and Scott have performed bilateral adrenalectomy in prostatic cancer in four patients who survived 1½, 1½, 11, and 116 days with adequate therapy of adrenal cortical extract desoxycorticosterone acetate and plasma transfusions given frequently

The Adrenal Glands

The adrenal or suprarenal glands lie at the upper pole of the kidneys. The two glands together weigh about 10 to 12 grams. They are richly supplied with blood by the superior suprarenal artery (from the inferior phrenic branch of the aorta), the middle suprarenal (directly from the aorta), and the inferior suprarenal (from the renal artery). The capsule contains the arteries, a nerve plexus, and some collections of sympathetic ganglion cells and sends a fine network of reticular fibers into the cortex, along with the capillaries. The capillaries empty into anastomosing sinusoidal blood spaces, which in turn drain into the central veins, which unite and emerge as a single vein. This empties into the inferior vena cava (right) and the renal vein (left). The sinusoids in the cortex are lined with endothelial cells and macrophages. About twenty to thirty nerves enter each gland, most of them coming from the celiac sympathetic plexus, some from the greater splanchnics, and a few from the vagus.

The glands are divided into a cortex and medulla. The latter contains chromaffin and sympathetic ganglion cells. The cortex develops from the mesoderm of the Wolffian ridge; the medulla from ectoderm, which gives rise to the sympathetic ganglion cells.

The medulla elaborates adrenaline (epinephrine, adrenin, or suprarenin). The effects imitate those of stimulation of the sympathetic nervous system and are, therefore, said to be sympathomimetic. The sympathetic fibers liberating an adrenaline-like substance (sympathin) are said to be adrenergic, that is, postganglionic fibers to the heart causing cardioacceleration and to blood vessels causing vasoconstriction, etc., as distinguished from those fibers of the parasympathetic and sympathetic (to sweat glands, vasodilators, and to adrenal medulla) which liberate acetylcholine and are called cholinergic (see Chapter 18). Some of the more important actions of adrenaline are: (1) Blood vessels are affected in different ways, depending on their location. Arterioles and capillaries of the skin, mucous membranes, splanchnic viscera (except the intestinal vessels) are constricted; the vessels of skeletal muscles, the coronaries, and the intestines are dilated. (2) The heart is slowed by adrenaline, but since this effect is produced through the carotid sinus and aortic nerves as a result of elevated blood pressure, it cannot occur where there is a great loss of blood volume. (3) Plain muscle is inhibited (stomach, intestine, bronchiole, wall of urinary bladder) so that intestinal movement is inhibited, bronchioles are dilated, and the urinary bladder does not contract, whereas the trigone and sphincter do sometimes, causing urinary retention. Muscles of the gall bladder, ureter, and pyloric, ileocolic, and anal sphincters are excited. Skeletal muscle shows a delay in fatigue. (4) Respirations are increased in rate and depth. (5) Carbohydrate metabolism is increased and hyperglycemia and glycosuria result due to mobilization of sugar from the liver, decreasing its glycogen as well as that of muscles. (6) General metabolism is also increased. The adrenal medulla is not essential to life. Dibenamine hydrochloride (dibenzyl-beta chloroethylamine hydrochloride) is an adrenolytic drug blocking the effects of adrenaline and is therefore useful in the diagnosis and treatment of diseases of the medulla producing excessive amounts of adrenaline, such as the pheochromocytomas. Any of the benzodioxan derivatives are useful as indicators of excess epinephrine since they lower the blood pressure due to this hormone but do not lower it in essential hypertension. The injection of .05 mg. histamine intravenously will precipitate a hypertension crisis in pheochromocytoma perhaps due to the vasodilation and increased amounts of adrenaline thrown into the circulation.

The emergency theory of epinephrine secretion holds that since it is secreted in greater amounts during nervous excitation, it is needed to make the body more efficient (in energy spending) during such crises (Cannon). The tonus theory assumes that the sympathetic nerve endings are being stimulated continuously, thus keeping up

of high fever, rapid respiration, purpura, convulsions, cyanosis, vomiting, and diarrhea the adrenals may be suspected.

Inflammations of the adrenals may be due to syphilis or tuberculosis, giving rise to Addison's disease if extensive. In the presence of severe septicemia from any cause but particularly from the meningococcus, hemorrhagic phenomena occur which include hemorrhage into the adrenal as well as the skin and other organs. The symptoms and signs resemble those of hemorrhage in the adrenals of infants and is known as the Waterhouse-Friderichsen syndrome. The symptoms are probably due to shock and overwhelming sepsis rather than to adrenal insufficiency.

Tumors of the Adrenal Glands

Neoplasms of the *adrenals* may be primary or secondary. The latter are very rare and occur as a result of metastases or invasion from the adjacent organs. Primary neoplasms may be derived from the various constituent tissues of the adrenal such as connective tissue (fibroma), fat (lipoma), nerves (neuroma, neurofibroma), muscle (myoma), blood vessels (hemangioma), lymph vessels (lymphangioma), and malignant tumors such as sarcoma and melanoma.

A second group of tumors peculiar to the ectodermal sympathetic nerve system are derived from the *medulla* of the gland. They are classified according to the type cell from which they are derived: (1) sympathoblastomas from embryonic cells; (2) ganglioneuromas from mature ganglion cells; and (3) pheochromocytomas from pheochromocytes or paragangliomas from mature chromaffin cells which are functionally active and which produce epinephrine. A third group of tumors originate from the adrenal cortex and are hyperplasias, adenomas, or carcinomas. They may occur (1) with no recognizable hormonal changes, (2) from changes due to hormonal influence or secondary sex characters (adrenogenital), (3) from changes due to hormonal influence on various metabolic processes (adrenometabolic tumors) (Cushing's syndrome), (4) from a mixture of (2) and (3); cortical tumors may occur in accessory adrenals (Marchand's bodies) which may be in the perirenal fascia or retroperitoneal fascia within the broad ligament attached to the ovary or testes.

Benign and malignant tumors from the framework of the adrenal are difficult to diagnose and are apt to be missed unless they are large enough to be felt. Malignant neoplasms may give no localizing signs or symptoms. A gradual loss of weight and strength, a progressive unaccountable anemia, and loss of appetite make one think of malignancy. In the absence of any demonstrable change, the retroperitoneal space with its adrenal may be the hidden site of the cancer.

Tumors of the Medulla.—The sympathogonia or the primitive cell of the sympathetic nervous system may differentiate into the sympathoblast, the sympathetic ganglion cells, and also the chromaffin cells (pheochromoblast and pheochromocyte). The whole group of tumors from

in large amounts. Inadequate therapy resulted in hyperpyrexia, hypotension, and addisonian pigmentation. There were also a reduction of 17-ketosteroids and urinary androgens as measured by the cock's comb growth technic, but a continued excretion of small amounts of estrogen.

Operations such as denervation, unilateral extirpation, bilateral subtotal resection, and irradiation of the adrenals have been done for such conditions as hypertension and other circulatory disorders, diabetes, peptic ulcer, hirsutism in the female, epilepsy, hyperthyroidism, Raynaud's disease, neurocirculatory asthenia, etc. The rationale is not clear, and the results in most cases are questionable.

Tests of Adrenal Cortical Function

The *ketosteroids* have been used as indicators of adrenal gland activity. Of those steroids found in the adrenal, those which have a keto group on carbon 3 are the ones which possess adrenal cortical function. The adrenal ketosteroids that have action on sexual characteristics are those with a distinctive side chain on carbon 17. These are known as the 17-ketosteroids and are derived from the adrenal cortex and the gonads, two-thirds from the former and one-third from the latter. The normal amount in a twenty-four hour specimen of urine for a child up to 10 years of age is 1 mg.; at puberty, in the male, 10 to 20 mg.; in the female, 9 to 15 mg. If the 17-ketosteroids is 30 mg. or over, the lesion is probably adrenocortical carcinoma. If above normal but under 30 mg., a diffuse or nodular hyperplasia of the adrenal is present. If there is evidence of associated hyperpituitarism, it is probably a hyperplasia. In the presence of a feminizing tumor of the male adrenal cortex, there is no increase in the 17-ketosteroids but estrogenic substances are increased.

The 17 ketosteroids have been divided into alpha and beta fractions, and data have been collected upon the relative importance of the beta fraction which is greatly increased in adrenal cortical adenoma or carcinoma. This is a great help in those cases of masculinizing changes. The 11-oxycorticosteroids with a 17-hydroxyl group are an index of the rate of secretion of adrenal cortical hormones influencing protein and carbohydrate metabolism. They are excreted in large amounts in patients suffering from burns, Cushing's syndrome, and adrenal cortical virulism.

Pituitary adrenocorticotropic hormone, when injected into normal persons (25 mg.), causes a decrease in circulating eosinophiles and a rise in excretion of uric acid. Patients with adrenal cortical disease fail to show these changes. Expressed as a ratio between uric acid and creatinine, a decrease of 50 per cent or more indicates adequate adrenal cortical reserve.

Sex homones. In the adrenogenital syndrome an excess amount of male hormones (androgens) has its effect on the secondary sex organs as shown in the masculinization of females (adults and children) and male maturity in male children. Hyperplasia and tumor cells may elaborate excessive amounts of steroids with female hormone activity (estrogens), causing femininism in males and early maturity in females.

The use of *air insufflation* in the perirenal area for x-ray studies and the retrograde pyelogram may help find a tumor of the adrenal (medulla or cortex) which cannot be felt. Thus with a careful clinical study of symptoms and signs in addition to the demonstration of a tumor in the region of the adrenal gland, a diagnosis may be made. The tests for function will help to differentiate the particular type of disease or neoplasm of the adrenal.

Diseases and Injuries of the Adrenal Glands

Injuries to the adrenal gland occur at birth and rarely in adult life. At birth, hemorrhage into the adrenal may result in death and the diagnosis is made at autopsy in almost every case, although in the presence

photungstic and acid hematoxylin stain. The growths are usually seen in the first few years of life and are often not recognized until metastases have occurred. Sometimes a tumor may be felt in the loin before metastases have occurred. In such instances a Wilms' tumor is also thought of. Intravenous pyelograms and even retrograde pyelograms may help make the diagnosis. Since the adrenal is outside and the Wilms' tumor inside the kidney, a greater distortion of the kidney, pelvis, and calyces is seen in the latter. In either case the treatment is complete removal of the adrenal and kidney (which may be invaded) through a transabdominal approach which is the best method of treatment. This permits preliminary ligation of the blood vessels before handling so that malignant cells may not be dislodged. The prognosis is poor and the cells are not radiosensitive.

The *ganglioneuromas* and *neurocytomas* arise from the adrenals, ganglions, Zuckerkandl's organ, coccygeal and carotid body. They vary in malignancy but are usually benign. They are symptomless and are discovered accidentally during physical examination. They should be removed surgically.

Pheochromocytoma (chromaffinoma) are hormonal tumors of the adrenal medulla. They arise in chromaffin cells anywhere, and though usually single, they may be multiple. Microscopically the tumors show excess of pheochrome cells with increase of interstitial stroma and ganglion cells. They may be benign or malignant. Clinically the neoplasms are seen in young or middle adult life, but no age is immune. The usual symptom complex is described as paroxysmal hypertension which is thought to be due to a temporary release of excessive amounts of epinephrine; in severe and sustained release of pressor substance, the symptoms resemble essential hypertension. The symptoms come on after excitement or physical stress or may at times be produced by massage of the tumor. Attacks start with palpitation, headache, epigastric pain, coldness of the hands and feet, and a fear of impending death. The systolic and diastolic blood pressures are increased but fall to normal after the attack. After the attack there is fatigue, perspiration, and exhaustion. Blood and urine tests show hyperglycemia and glycosuria which do not respond to the usual treatment of diabetes. The diagnosis depends on the history and clinical findings; additional evidence includes a mass which is often felt; symptoms and signs of pheochrome syndrome in so-called essential hypertension; reduction of blood pressure by an epinephrine antagonist such as benzodioxan; precipitation of an attack by histamine and evidence of the tumor if it cannot be felt by pyelography or scout films or perirenal air insufflation. The syndrome must be differentiated from hyperthyroidism, diabetes, and psychoneurosis. The treatment is surgical removal by the transabdominal route. This permits exploration for other unrecognized tumors and, more important, it allows for preliminary ligation of all vessels before manipulation is started. If the diagnosis of adrenal tumor is certain, a lumbar

the sympathogoma are the most common neoplasms of the abdominal cavity in childhood. There are four types: (1) sympathogonioma from the embryonic sympathiogonia—extremely malignant; (2) sympathoblastoma or neuroblastoma sympatheticum, the most common of the group; also highly malignant; (3) the benign ganglioneuroma; and (4) the chromaffinoma or pheochromocytoma which is an adrenaline secreting tumor.

Fig. 399.—Carcinoma of the adrenal cortex. Woman aged 33 years. Note the virilism and hirsutism.

The *sympathoblastomas* occur in either sex and may arise not only from the adrenal glands, but also from the retroperitoneal or retropleural sympathetic ganglion and even the cervical region. Their rapid growth and rapid spread by the lymphatics and blood stream permits early invasion of the liver (Pepper syndrome), the skull and orbits (Hutchinson syndrome), or any organ or tissue in the body. The microscopic picture is one of a highly cellular and infiltrative neoplasm with cells not unlike large lymphocytes forming occasional rosettes, with the nuclei peripherally placed. Neurofibrils can be seen with the phos-

Hormonal tumors (Cahill) are divided into those which produce changes due to (1) excess androgens—in a girl toward adult masculinity; in a boy toward adult masculinity; (2) excess estrogens—in a man toward femininity. Androgenic tumors in a girl cause changes described as pseudohermaphroditism. Usually the cause is bilateral hypertrophy of the adrenal cortex rather than unilateral tumor. There is a hypertrophy of the clitoris, hair on the genitals, deep voice, good muscular development. Older girls do not menstruate, have hirsutism, a deep voice, and early closure of the epiphyses. *In women there is a suppression of*

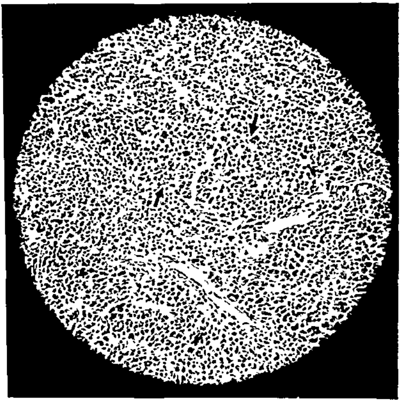

Fig. 401 —Carcinoma of the adrenal cortex. Arrows point to an area showing neoplastic cells.

female characteristics and the appearance of male secondary sex patterns: hirsutism, enlarged clitoris, cessation of menses, acne, low voice, recession of breasts, labia, and uterus. These changes are known as the adrenogenital syndrome. Laboratory studies show increase of androgens in the urine and also the 17-ketosteroids. *X-ray* with *insufflation* of air in the perirenal space may reveal the tumor, although this is not an innocuous procedure. The tumors may be adenomas or adenocarcinomas. The excessive granular-cell cytoplasm has given the name of "granular-cell tumors" to this group. The treatment is surgical extirpation if tumor is present and the results are usually good.

incision may be used. This may be bilateral if the diseased gland is not found on the first side exposed. If exposure is inadequate through the ordinary incision used for operations on the kidney, the eleventh and twelfth ribs may be resected. Still more room may be obtained by resecting a portion of the tenth rib. The pleura may be pushed forward and the diaphragm incised. In this way, the pleural cavity is not opened. After removal there is an immediate fall in blood pressure, requiring the use of epinephrine. Recurrences are due to incomplete removal, the presence of other tumors, and functionating metastases.

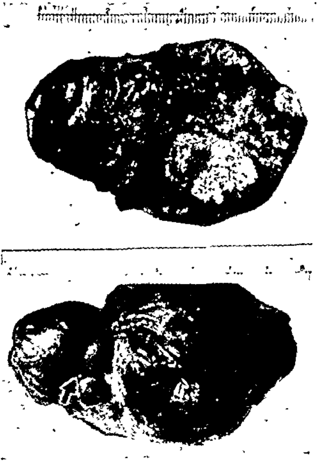

Fig. 400.—Carcinoma of the adrenal cortex. Arrow points to a groove between the normal gland on the left and the tumor on the right.

Tumors of the Adrenal Cortex.—*Nonhormonal tumors* are encapsulated but usually malignant. They are irregular and yellowish, and the large vacuolated cells that are found do not contain steroids as a rule. They are usually silent and are not discovered until they are felt on routine examination or until, because of their size, they produce pain. If malignant, metastases may be recognized first. Often they are mistaken for tumors of the tail of the pancreas. The treatment is complete removal by a transperitoneal approach. Since they are usually encapsulated, their removal is not difficult as a rule.

gastric or pelvic plexus, the ovarian plexus, and the uterine nerves. Afferent impulses from the ovary reach the central nervous system through the posterior root fibers of the tenth thoracic nerves. The ovaries present a pock-marked appearance due to the fact that the ovum develops in the germinal epithelium of the ovarian cortex within the *Graafian follicle.* The germinal epithelium sends small groups of cells into the ovarian stroma. One cell of the group is the *primordial follicle* which migrates deeper into the stroma which in turn produces two layers of cells to surround the follicle—the fibrous outer theca externa and the inner vascular and more cellular theca interna. The follicle ruptures and extrudes the ovum during the middle third of the menstrual cycle. The small pit which remains fills with *luteal* cells and fibroblasts, forming what is known as the *corpus luteum,* which may be true *(corpus luteum verum)* if pregnancy occurs, or false *(corpus albicans),* ending in fibrous tissue after ten days if the ovum has not been fertilized. Some animals do not have a corpus luteum (monotremes, such as the platypus, or duckbill). If the corpus luteum is removed in the early months of pregnancy, abortion usually follows. This is not true if it is removed in the later months. The granulosa cells of maturing Graafian follicles and also the cells of the corpus luteum give rise to a hormone (the *follicular hormone* or *female sex hormone, oestrin*) which is concerned with the initiation of menstruation and the secondary sex characteristics; the lutein cells of the corpus luteum gives rise to the hormone *progesterone,* which induces changes in the uterine mucosa preparatory to ovum implantation, helps in the formation of the placenta, stimulates growth of the mammary glands, and suppresses menstruation and ovulation during pregnancy. Progesterone has also been termed the "nidification" hormone, because after implantation of the ovum, the hormone of the corpus luteum is necessary for the development of the maternal "placenta" (the decidua). Oral temperatures vary during phases of the menstrual period, being low during the first part of the month, dropping to a minimum about the time at which ovulation occurs, and rising to a relatively high level until the next menses, when it drops abruptly. If conception occurs it remains at the high postovulation level. One hypothesis for the phenomenon is that the rise is brought about by ovulation and the elevated basal temperatures are maintained by corpus luteum activity. It is important to note that the ovaries are in intimate relationship with other endocrine glands. This is especially true of the pituitary (anterior lobe), which may, through its gonadotropic hormone, stimulate the follicle (prolan A) or the corpus luteum (prolan B) into activity and secretion and stimulate the secretion of milk by the hormone *prolactin,* the lactogenic hormone. Androgenic hormones from the adrenal cortex oppose and perhaps also act as pacemakers to the female sex hormones.

Diseases of the Ovaries

Congenital anomalies of the ovaries, unlike the rest of the reproductive system, are not common. There may be absence of one or both ovaries, or they may be hypoplastic, giving rise to incompletely developed secondary sex characteristics. The ovaries may fail to descend, or there may be accesory ovaries. Rarely there is inclusion of aberrant glandular tissue such as thyroid or adrenal, and still more rare is the inclusion of testicular tissue (ovatestes).

Inflammations of the ovary (oophoritis) are due usually to an extension of the fallopian tube inflammations. These may be acute or chronic; the former are initiated usually by the gonococcus, streptococcus, and staphylococcus, the latter by the tubercle bacillus, the spirochete, and actinomyces (see Chapter 23).

In a boy there is early puberty (pubertas praecox) with early enlargement of the genitals, hair on the face, great muscular development (infant Hercules). Sometimes there is a mixed picture with obesity and redness of the face (Cushing's type). If a tumor is found, it should be removed, but substitution therapy may be necessary for a while because the opposite adrenal is usually atrophied. The results are good.

Excess estrogens in a man due to adrenocortical tumors cause a decrease in size of the genitals, enlargement of the breasts and nipples, and impotence. The tumors are usually carcinoma and should be removed. *Cushing's syndrome* has been described previously in this chapter under basophilic adenoma of the pituitary. Adrenal tumor may also cause it. (Symptoms and signs are painful obesity of the face, neck, and abdomen with purple striae on the abdomen and thighs, acrocyanosis, hirsutism, polycythemia, glycosuria, muscular weakness, osteoporosis, amenorrhea in women, impotence in men. The syndrome is usually seen in women and is usually due to bilateral adrenocortical hypertrophy "foam cell adrenals." Tumors may be the cause and are usually adenomas. Operative removal is indicated, but it may be followed by acute adrenal insufficiency because the opposite gland is atrophic. The preoperative preparation includes adrenocortical extract (20-50 c.c.) the day before surgery, and this is repeated in the morning before operation. In addition, 1000 c.c. of physiological saline with vitamin C is given intravenously. Sodium citrate has been advised to fix the salt. This treatment is continued for several days after surgery. Sometimes desoxycorticosterone acetate (5-10 mg.) is also given by intramuscular injection.

The surgical approach may be through the abdomen or by the lumbar route as described under Pheochromocytoma. If the diagnosis of adrenal tumor is fairly certain, the latter is preferable and may be bilateral if the incorrect side has been explored first.

Ovaries

The ovaries are derived from the embryonic genital glands (gonads) which in the male give rise to the testes. At six weeks the sexless gonads consist of a superficial germinal epithelium and an internal epithelial mass. At eight weeks the gonads begin to assume the characteristics of testes or ovary. Although in the embryo the ovaries lie rather high in the abdomen, they descend later to their permanent position, due to the gubernaculum of Hunter (round ligament), which fails to keep pace with the growth of the rest of the body. This results in such traction on the ovary that it pulls it down into the pelvis. The ovaries are bilaterally situated in the pelvis, are held in place by the tubo-ovarian ligaments, and are nourished by the ovarian arteries, which are branches of the abdominal aorta. The ovarian veins anastomose freely, forming the pampiniform plexus, finally forming two veins which accompany the corresponding ovarian artery, ultimately fusing into one vein which empties into the vena cava on the right and the left renal vein on the left. The lymph vessels of the ovary join with those from the upper part of the uterus and end in the precaval and laterocaval nodes on the right and the lateroaortic and preaortic nodes on the left. The nerves are derived from the hypo-

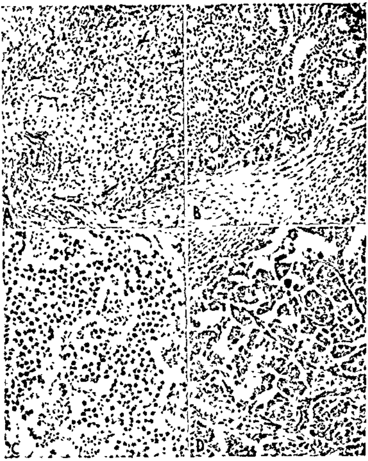

Fig. 402.—Photomicrographs of solid tumors of the ovary. *A*. Theca-cell tumor. Cells are derived from the theca interna. Most of the cells resemble those of connective tissue. Areas such as are shown are yellow spots in which the cells have *undergone luteinization* and produce an excess of progesterone. *B*. Arrhenoblastoma of the ovary. *Note* the adenomatous arrangement of the tumor, which is surrounded by connective tissue. *C*. Dysgerminoma of the ovary. Note the lack of differentiation in the cells, which are polygonal in shape and contain many mitotic figures and *very little stroma*. *D*. Carcinoma of the *ovary*. *Note the ad*enomatous arrangement of the growth, which has very little stroma and much variation in size and shape of its cells.

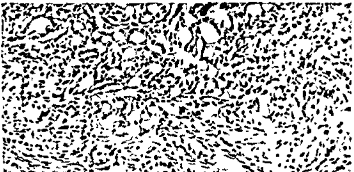

Fig. 403.—Krukenberg tumor of the ovary. This section resembles glandular tissue (adenocarcinoma). Note "signet ring" cells.

Tumors and Cysts of the Ovary

Tumors and cysts of the ovary are discussed in Chapter 23.

Here we shall enumerate the various types of new growth in the pluripotential ovaries and discuss those which stimulate the ovary to incomplete or perverted function, which decrease the natural secretion, or which increase or revitalize the depressed function.

A. Cystic ovarian tumors
  1. *Simple cysts*
    a. *Graafian follicle*
    b. *Theca luteum*
    c. *Corpus luteum*
    d. *Endometriosis* (chocolate cysts are not all due to endometrioses but are more often due to hemorrhagic follicle or corpus luteum cysts)
    e. Germinal inclusion (very small cysts beneath the germinal epithelium and lined by cells similar to those covering the ovary)
  2. Cystadenomas
    a. Serous (bilateral in 30 per cent of the cases; papillary types are apt to become malignant)
    b. Pseudomucinous (usually unilateral papillae in about 6 per cent and malignant degeneration in about 5 per cent of the cases; intraperitoneal transplants produce pseudomyxoma)
  3. Dermoid cysts (containing skin, hair, teeth, nails) and teratomas which may contain any tissue or organ; malignant transformation may occur (epithelioma and even melanoepithelioma in dermoids and almost any type in termatomas)

B. Solid tumors
  1. Nonfunctioning
    a. Fibroma
    b. Brenner tumor
    c. Adenocarcinoma
    d. Sarcoma
    e. Teratoma
    f. Krukenberg tumor (usually from stomach)
    g. Mesonephroma (resembling mesonephric tissue)
    h. Secondary tumors (carcinoma, sarcoma)
  2. *Functioning*
    a. *Granulosa cell*
    b. *Arrhenoblastoma*
    c. *Dysgerminoma*
    d. *Theca-cell*
    e. *Aberrant*
      (1) Adrenal adenoma—masculinovoblastoma; the tumor resembles adrenocortical tissue and gives symptoms like arrhenoblastoma plus hypertension, polycythemia, and a tendency to diabetes and obesity
      (2) Thyroid tumor of the ovary—struma ovarii—probably from a teratomatous growth; usually found as an adenoma and may become malignant
    f. Metastatic chorionepithelioma from uterus (or primary in ectopic pregnancy of tube and ovary or in teratoma)

The granulosa-cell tumor arises from fetal rests of *granulosa* cells and becomes a firm encapsulated growth. If it occurs *before* puberty, it may cause *sexual precocity;* if after the menopause, rejuvenation. Dur-

TABLE XXIX

SOLID TUMORS—COMPARATIVE DATA ON SOME OF THE MORE COMMON "NONFUNCTIONING" TUMORS OF THE OVARY
(Modified from Dockerty: Proc. Staff Meet., Mayo Clin., 1941)

	PRIMARY ADENOCARCINOMA	SARCOMA	TERATOMA	KRUKENBERG'S TUMOR	FIBROMA	BRENNER TUMOR
Histogenesis	Probably begin as cystic tumors (cystadenomas)	60% from fibromas; 40% from stroma of ovary	Mutation of cells or rests (?)	Always metastatic; stomach (80%), jejunum, colon, gall bladder, breast, hepatic duct, uterus	Ovarian stroma	Embryonic rests (?), teratomatous origin (?), mutation of cells (?)
Age	Any age	Any age—usually earlier than carcinoma	Any age—usually less than 10 or more than 40 years	Usually less than 45 years	100% after puberty	70% after menopause
Characteristic symptoms or syndrome	Rapidly growing tumor; cachexia; frequently ascites	Nonspecific	Nonspecific	Often gastric	Slow-growing tumor; ascites in 10% with large tumors; occasionally also hydrothorax*	Symptoms not characteristic
Unilateral or bilateral	50% bilateral	20% bilateral	15% bilateral	25% bilateral (small tumors); 85% bilateral (large tumors)	90% unilateral	95% unilateral
Gross appearance	Solid, brown, often adherent; often necrotic and cystic	Not diagnostic	Variety of tissues found	Solid smooth surface; cut surface becomes concave	90% solid, white	70% solid, resembling fibroma; 30% solid nodules in walls of pseudomucinous cysts
Microscopic pattern	Malignant cells with tendency to formation of glandular spaces	Usually fibrosarcoma	Heterogenicity of tissues	Often signet-ring cells	Cellular and fibrous types; small fibroblastic cells	80% fibrous stroma; 20% squamous cells in islands with cystic centers; mucus
Prognosis	Malignant	Malignant	Sometimes malignant	Malignant	Benign (if not fibrosarcoma)	Benign
Hormone elaborated	No hormones	No hormones	?	No hormones	No hormones	No hormones

*This also may occur with other large tumors of the pelvis.

TABLE XXVIII

SOLID TUMORS—COMPARATIVE DATA ON SOME OF THE MORE COMMON "FUNCTIONING" TUMORS OF THE OVARY
(Modified from Dockerty: Proc. Staff Meet., Mayo Clin., 1941.)

	FEMINIZING	MASCULINIZING	NEUTRALIZING	FEMINIZING
	GRANULOSA-CELL TUMOR	ARRHENOBLASTOMA	DYSGERMINOMA	THECA-CELL TUMOR (THECOMA)
Histogenesis	Granulosa cells	Testicular "rests"	Undifferentiated sexual cells	Theca of follicle
Age of patients	40 to 60 years (60%)	20 to 40 years (90%)	5 to 20 years (70%)	80% after menopause
Characteristic symptoms of syndrome	Precocious menstruation, early development of secondary sexual characteristics, postclimacteric menstruation, feminization	Sterility, hirsutism, atrophy of breasts, hypertrophy of clitoris, voice changes, amenorrhea, masculinization	Pseudohermaphrodism (can have normal menstruation and pregnancy), hypo plasia of genital organs	Often periodic postmenopausal bleeding (as in granulosa-cell tumors)
Unilateral or bilateral	Unilateral (95%)	Unilateal (100%)	Unilateral (65%)	100% unilateral
Gross appearance	Solid, granular, homogeneous	Solid, multicentric nodules	Solid; consistency of brain	Solid, yellow, fibrous; uterus large
Microscopic pattern	Folliculoid, cylindroid, diffuse	Tubular, cylindroid, and diffuse with interstitial cells	Undifferentiated cells, giant cells, lymphocytes; all neoplasms, grade 4	Fibroblastic cells laden with fat; hyaline bands
Five-year survival	95 per cent	75 per cent	60 per cent	Sometimes malignant
Hormone elaborated	Estrogen and progestin?	Male sex hormone	No hormones	Estrogens; so much that gonadotropic hormone of pituitary inhibited and no prolan B

ductules. These pierce the tunica albuginea and enter the caput epididymis where after much twisting the little canals finally open into the duct of the epididymis. This duct is 19 to 20 feet long, beginning in the head of the epididymis and after a tortuous course ending at the tail, becoming the ductus deferens. The testis is supplied by the internal spermatic artery which is a branch of the aorta. The veins form the pampiniform plexus which finally pours into the spermatic vein which ends in the inferior vena cava on the right and the left renal vein on the left side. The lymph vessels pass upward in the spermatic cord and empty into the right and left lateroaortic and preaortic nodes also the external iliac nodes. The nerves are derived through the aortic and renal plexuses from the tenth thoracic segment of the spinal medulla. Afferent fibers from the epididymis reach the spinal medulla through the posterior roots of the eleventh and twelfth thoracic and first lumbar nerves. The arteries and nerves and lymphatics communicate with those of the lower part of the ductus deferens (artery of the ductus and nerves of the hypogastric plexus). The descent of these organs from within the abdominal cavity into the scrotum is discussed in Chapter 20. Here it was pointed out that (1) the gubernaculum descends first, "pulling" the testis down, and (2) as the gland descends, it pulls the layers of the abdominal wall and peritoneum with it, and these, together with the peritoneum (tunica vaginalis), form the covering of the cord and testis, respectively.

The seminiferous tubules are coiled and twisted. They are lined by several layers of epithelial cells derived from germinal epithelium. These cells give rise to the spermatozoa. The epithelial lining of the tubules corresponds to the stratum granulosum of the Graafian follicle. *The youngest cells (spermatogonia)* lie near the basement membrane, and next, toward the lumen, are the *spermatocytes*, which divide to form the *spermatids*, which are transformed into the *spermatozoa*.

The anterior pituitary, through its gonadotropic hormone, stimulates the spermatogenic cells. The cells of Sertoli, lying among the spermatogonia, are supporting and nourishing cells. The interstitial cells (cells of Leydig) are supposed to elaborate the male sex hormone and in turn are said to be stimulated by the luteinizing hormone of the anterior pituitary.

The male hormone *(testosterone, androsterone)* has been isolated and can be obtained in crystalline form. Chemically it belongs to the sterols. It stimulates the formation of secondary sex characteristics.

Another hormone, *inhibin*, is supposed to exert an inhibitory effect on the prostate by acting on the pituitary and causing the latter to decrease its effect on the interstitial cells of the testes. As the testes undergo atrophy, inhibin is decreased, and consequently the gonadotropic hormone is liberated in greater amounts and causes a hypertrophy of the prostate.

A hormone does not stimulate the gland which secretes it and therefore testosterone does not stimulate the interstitial cells. It does have a salutary effect, however, in underdevelopment of the sex organs, and increased libido following its administration has been reported. The anterior pituitary-like hormone derived from pregnancy urine has also been used with reported success in cryptorchidism, sterility, and underdevelopment.

Congenital Anomalies

Congenital anomalies of the testicles are common. Among the more common are as follows: (1) Cryptorchidism (see Chapter 20) or nondescent; may be associated with hernia. If present on one side, it is known as monorchism; if both sides, anorchism. Cryptorchidism, if bilateral, gives rise to hypogonadism because the seminiferous tubules degenerate (perhaps as a result of the high intra-abdominal temperatures, but the interstitial cells remain. Therefore, subjects with an-

ing the menstrual life of a woman, *metrorrhagia* may occur. In other words, it stimulates the formation of the female sex hormone (the follicular hormone, or oestrin).

Arrhenoblastomas exert a "masculinizing" effect (virilism). They develop from potentially testicular cells present in the rete ovarii, and through their hormonal effects override the feminine influence of the ovary. These growths are unilateral as a rule and of low-grade malignancy. Removal of the growth may cause complete disappearance of symptoms (hirsutism, amenorrhea, bass voice, hypertrophied clitoris, etc.).

Dysgerminoma corresponds to seminoma of the testis. It is highly malignant and leads to an arrest of secondary sex characteristics.

Tables XXVIII and XXIX set forth comparative data on the more common solid tumors of the ovary.

The treatment of ovarian neoplasms is surgical for the following reasons: (1) In benign growths to prevent twisting, great increase in size, or malignant transformations; (2) in functioning growths to alleviate "hormonal" symptoms as well as the reasons given in (1); (3) in malignant growths to prevent spread and metastases. Functioning neoplasms require the opposite ovary to restore normalcy after their removal; therefore only the affected side is removed, leaving also the uterus and tubes. Carcinomas require extensive removal, including the opposite ovary, tubes, uterus, and nodes of the first echelon. X-ray treatment should be used in cases with peritoneal implant or lymph node involvement. Androgenic hormones may be helpful in the relief of pain.

Testes

The embryological development of the testes is the same as that of the ovary until about eight weeks; then the male genital glands become more compact and the original broad attachment to the mesonephros becomes the mesorchium or the gonadal mesentery. There appear in 14 mm. embryos branched anastomosing strands of cells—testes cords; also a layer of tissue between the germinal epithelium and the centrally located testes cords which will become the tunica albuginea or fibrosis capsule. The testes cords converge toward the mesorchium as the primordium of the rete testis. Soon the rete primordium becomes a network of strands which unite with the testes cords, each of which will split into three or four daughter cords to form the forerunners of the seminiferous tubules which do not canalize until about the seventh month. The testis of the newborn shows hypoplasia perhaps due to maternal hormones during pregnancy.

Beneath the serous tunica vaginalis the testis is covered by the tunica albuginea, which sends strands (septula testis) into the organ, dividing it into wedge shaped lobules (lobuli testes) and joining posteriorly to form the mass of fibrous tissue known as the mediastinum testis (corpus Highmori). This structure is traversed by the rete testis, arteries, veins, and lymph vessels. The parenchyma is made up of the convoluted seminiferous tubules (tubuli seminiferi contorti). There are three to four tubules to each lobule (a total of 600 to each gland); after a course of about two feet, they end in straight fine canals (tubuli seminiferi recti) and empty into the rete testis. Secretion of the seminiferous tubules is carried from the rete to the canal of the epididymis through from fifteen to twenty tubules called ductuli efferentes testis or efferent

Tumors of the Testicle

1. Supporting structure
   a. Hemangioma
   b. Fibromas
   c. Lipoma
   d. Neurofibrosarcoma
   e. Melanoblastoma
   f. Lymphosarcoma
2. Tumors of germ-cell origin
   a. Semenoma
   b. Undifferentiated or adenocarcinoma
   c. Trophocarcinoma from cytotrophoblast
   d. Chorioepithelioma from syncytotrophoblast
   e. Teratoma with undifferentiated carcinoma or adenocarcinoma
   f. Teratoma with trophocarcinoma
   g. Teratoma with chorioepithelioma
   h. Teratoma (adult type)
3. Tumors of the interstitial cells of Leydig
4. Metastatic neoplasms

Fig. 404.—Teratoma of testicle in a man aged 25 years. There were metastases in lungs and retroperitoneal tissues. The Aschheim-Zondek test was positive: 500 mouse units of prolan A per liter.

Neoplasms of germ cell origin comprise 90 per cent of all testicular neoplasms ordinarily encountered and therefore deserve special consideration.

Semenoma is seen in older men, in persons with cryptorchidism, and in persons with atrophic testes. It metastasizes by the lymphatics and by permeation. The tumor is radiosensitive, and the prognosis is therefore hopeful. Treatment consists of orchiectomy by first tying the cord vessels. The radical operation is not necessary and often not feasible. X-ray therapy should be used following surgery.

orchism are sterile but are sexually otherwise normal. Malignant tumor formation is more common in undescended testicles than in those in the normal position. (2) Aplasia or hypoplasia. (3) Supernumerary testicle. (4) Adrenal or splenic inclusions. (5) Ovarian inclusion—ova-testis. (6) Hydrocele. Hydrocele is due to failure of the tunica vaginalis to obliterate. The cavity, which becomes filled with fluid, often communicates with the peritoneal cavity (hernia). The treatment of this is operative. In the congenital type it is best to wait until after 5 years of age because spontaneous obliteration sometimes occurs. After this age the tunica vaginalis is split, "turned inside out," and sutured (bottle operation).

Spermatocele is probably a retention cyst and, if large, should be excised. Varicocele is a dilatation of the spermatic veins in the pampiniform plexus. Excision often leads to "painful cord." If there is no obstruction above (from a renal tumor or pressure from other cause on the renal vein), scrotal support is used.

Injuries of the Testes

Injuries may be due to trauma or to torsion of the appendix, of the testes, or of the spermatic cord. A blow or crushing injury leads to hemorrhage and rupture of the tunica albuginea. It may be followed by infection or may result in scar formation so extensive that atrophy ensues. The relationship between injury and neoplasia is conjectural. Torsion is due to a long spermatic cord and gubernaculum in a capacious tunica vaginalis. Undescended testes may undergo torsion. The exciting cause is usually a strain (cough, sneeze, heavy lifting), but may occur without any known cause. If the torsion persists, venous return will be impeded and ultimately, when venous pressure equals arterial pressure, circulation ceases and gangrene occurs. The clinical symptoms and signs resemble an acute epididymitis or incarcerated hernia if the torsion is outside the tunica vaginalis. Prompt surgery will avert serious trouble. The operation is simple and requires only untwisting of the cord.

Inflammations of the Testes

(1) Acute nonspecific orchitis (from epididymitis, mumps, trauma, generalized infection); (2) tuberculosis—practically always secondary to tuberculosis of the epididymis; (3) syphilis—practically always primary in the testes (4) filariasis—affects the testes in more than 50 per cent of the cases; (5) actinomycosis—rare. Treatment consists of first the treatment of the primary disease. Locally, cold relieves pain in the acute inflammations. Penicillin and streptomycin are useful in all of the infections, the latter especially in tuberculosis. Aureomycin is also useful. Orchiectomy may be necessary in refractory cases with irreversible changes.

positive. They are radioresistant. Orchiectomy is done but the radical operation is usually not indicated because of distant metastases.

Teratocarcinomas may be monodermal or tridermal since they arise from totipotent sex cells. This group may include semenoma, embryonal carcinoma, choriocarcinoma, chorioepithelioma, or adult embryoma or teratoma. The treatment in this group is radical orchiectomy. X-ray treatment is ineffective.

Interstitial cell tumors are usually benign. Orchiectomy should be done, and if a study of the permanent section shows malignancy, radical resection may be done as a second stage operation.

Metastatic neoplasms are extremely rare. The presence of a painless mass in the testes should suggest new growth. In the *chorioma testis,* and perhaps in other teratomas, the Aschheim-Zondek or Friedman test may be positive. Although the growths mentioned, as well as those affecting the interstitial cells, should stimulate or decrease the function of these cells, it is extremely rare to find a growth affecting secondary sex characteristics as tumors of the ovary do.

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Adenocarcinoma or *undifferentiated* carcinoma grows rapidly and metastasize to the retroperitoneal nodes. It is not so radiosensitive and requires radical orchiectomy. This is done through an oblique incision extending from the costovertebral angle to the external inguinal ring. The internal spermatic vessels which lie between the transversalis fascia and peritoneum are ligated at their origins and terminations (aorta and vena cava and left renal vein). The dissection is carried down to where the vas turns down to pass along the posterior surface of the bladder. Nodes may be encountered along the spermatic cord, at the internal ring on the external iliac artery, at the bifurcation of the hypogastric artery, and between the common iliac artery and the genitofemoral nerve. On the right side nodes may be found on the anterior surface of the vena cava, between the vena cava and aorta, and at the junction of the spermatic vein and the vena cava. On the left side nodes may be found lateral to the aorta and at the junction of the spermatic vein and renal vein. Sometimes the kidney is sacrificed on the left to remove all metastases.

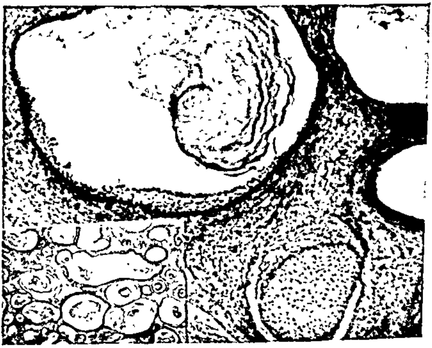

Fig. 405.—Teratoma of the testicle. Note the cystic areas as seen in the low power (lower left). Under high power, some of these are found to be lined with squamous epithelium (large upper cyst); others show cartilage (lower). Very little glandular structure is seen in this section.

Trophocarcinoma from the cytotrophoblast, which is the precursor of the syncytotrophoblastic cells of *chorioepithelioma*, constitutes a rapidly growing tumor which metastasizes early by the blood stream and the lymphatics.

Chorioepithelioma is composed of Langhans' cells and syncytium. There is rapid growth and early metastases by the blood stream and lymphatics. The Aschheim-Zondek and Friedman tests are frequently

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Chapter 23

REPRODUCTIVE AND URINARY SYSTEMS

The reproductive and urinary systems are closely related developmentally, anatomically, and functionally, also in their susceptibility to certain infections such as gonorrhea. Moreover, in the female, injuries to the birth canal frequently affect the bladder support, and pregnancy may interfere with normal kidney function. In both sexes congenital anomalies of either system may occur, thereby affecting the other. For these reasons the two systems are considered together in this chapter.

THE FEMALE REPRODUCTIVE SYSTEM

The female reproductive system is composed of ovaries, Fallopian tubes, uterus (body and cervix), vagina, and vulva. A description of the ovaries and their function is found in Chapter 22, Glands. Diseases and abnormalities of this system make up the special field of *gynecology* (literal meaning, "the study of women").

The two Mullerian ducts give rise to the uterine tubes (Fallopian tubes), the uterus, and the vagina. Congenital anomalies occur if these ducts fail to fuse (double uterus), if they only partially fuse (uterus bicornate), or if they fail to develop (congenital absence of vagina and uterus). In the indifferent stage of the embryo (both the male and the female), there are a pair of genital glands, a pair of mesonephric or *male* ducts, a pair of Mullerian or *female* ducts, and a genital tubercle bearing the phallus. Fig. 406 illustrates the changes which occur in the development of these structures in the male and the female. If nature errs in the sex development, true or false hermaphroditism may occur. The former is extremely rare and implies the presence of both ovarian and testicular tissue. The latter is not uncommon and implies the presence of one type of sex glands (either male or female) and the opposite type of secondary sex characteristics. (See also Fig. 410.)

The Fallopian tubes join the uterus on either side and are held in position by the tuboovarian ligaments. The ovum is fertilized in the tube and then descends into the uterus. This organ is held in position by three sets of ligaments: the broad ligaments, which are most important, the round ligaments, and the uterosacral folds. In front of the uterus lies the bladder, which is closely attached to its anterior surface. Behind is the rectum, separated from it by a space covered with peritoneum, called the pouch of Douglas. The *cervix uteri* extends into the vagina, and its external opening (external os) is easily seen with the speculum and is felt upon bimanual examination. The vulva is composed of the labia (major and minor) enclosing the vaginal orifice, just anterior to which is the urethral meatus. The blood supply of the ovaries is from the ovarian arteries (from the aorta); that of the round ligaments, from the arteries of the round ligaments (from the external iliacs). The uterus is supplied by the uterine arteries which arise from the hypogastrics (internal iliacs). These cross the ureters near the cervix and ascend toward the fundus.

The lymphatics of the cervix empty into the middle or medial groups of the external iliac chain; the hypogastric and common iliac nodes and the nodes of the promontory; those of the corpus terminate in the latero aorti nodes, the preaortic nodes in the vicinity of origin of the inferior mesenteric artery, in the nodes of the middle group of the external iliac chain, and sometimes in the superomedial superficial inguinal nodes.

The nerve supply is somatic (sensory and motor) by way of the lumbosacral plexus and visceral by way of the superior hypogastric (presacral) plexus which becomes the middle hypogastric plexus below the promontory, becoming, at the level of the first sacral vertebra, the inferior hypogastric plexus. Fibers from the sacral plexus which join the latter represent the parasympathetics and are known as the nervi erigentes. These are the source of parasympathetic innervation of the uterus, tubes, ovaries, and the walls and internal sphincters of the bladder and rectum. The plexus of the pelvis located on the posterior surface of the base of the broad ligament supplies sympathetic fibers to the uterus, bladder, vagina, and rectum, whereas the aortic plexus supplies fibers which run along with the ovarian arteries to the ovaries.

The uterus is composed of an external mesothelial layer (serosa), a middle layer composed of bundles of smooth muscle (myometrium), and an inner layer (endometrium). The vaginal portion of the cervix is stratified squamous epithelium, but at the external os it becomes nonciliated columnar epithelium which lines the cervical canal to the internal os and sends projections to form its compound racemose cervical glands.

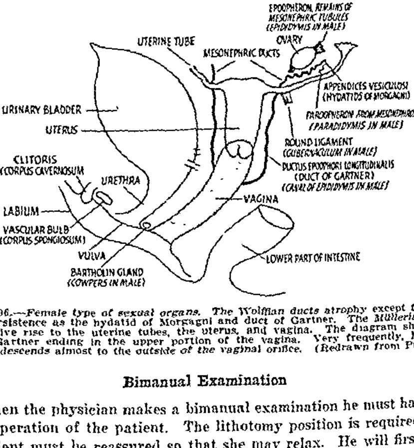

Fig. 406.—Female type of sexual organs. The Wolffian ducts atrophy except for occasional persistence as the hydatid of Morgagni and duct of Gartner. The *Müllerian ducts* fuse to give rise to the uterine tubes, the uterus, and vagina. The diagram shows the duct of Gartner ending in the upper portion of the vagina. Very frequently, however, this duct descends almost to the outside of the vaginal orifice. (Redrawn from Prentiss.)

Bimanual Examination

When the physician makes a bimanual examination he must have the full cooperation of the patient. The lithotomy position is required, and the patient must be reassured so that she may relax. He will first note the consistency of the cervix, whether hard and smooth (normal), soft and smooth (pregnancy), or hard and friable (neoplasm); also whether there are tears or neoplasms. Next he will palpate the lateral fornices for masses or swellings in the adnexa, then the posterior cul-de-sac for abscess or retroversion. Finally, he will note the position and mobility of the uterus. The speculum enables him to inspect the cervix, to take smears for bacteria or tumor cells, and, when necessary, to take tissue for biopsy.

Menstruation

Menstruation may be of the ovulatory or anovulatory (especially at the menopause) type. The latter shows no secretory changes in the endometrium. We have seen in Chapter 22 that the anterior lobe of the pituitary secretes a hormone which causes stimulation and maturation of the follicle and another which causes its luteinization after it ruptures. After menstruation, as the Graafian follicles begin to mature, estrogen is secreted and one follicle reaches maturity while the rest degenerate. The corpus luteum which forms secretes estrogen and progesterone. Estrogen alone causes proliferation of the endometrium; however, estrogen and progesterone cause differentiation or secretion and inhibit ovulation. When the corpus luteum degenerates menstruation ensues.

Menstruation is divided into the following phase: (1) Proliferative phase (follicular or interval phase) which corresponds with the ripening of the follicles and ends with ovulation (in twenty-eight day cycle occurs about fourteenth day). After menstruation the endometrium consists of thin basilar layers and a portion of the spongiosa. Soon epithelium develops from the underlying glands, which later changes from a few small straight structures to numerous elongated tortuous glands. The blood vessels are small, numerous, and engorged toward the end of the proliferative phase. (2) Secretory phase (differentiative, progravid, or progestational phase) which is due to the action of the corpus luteum secretion (fourteenth to twenty-sixth day of cycle). The endometrium *shows a basilar layer*, a spongiosa *(tortuous and dilated portion of* glands), and a compact layer where the glands are straighter and narrower. (3) Ischemic phase which occurs one to two days before menstruation and is due to a constriction of the special vessels that pass between the basilar and spongiosa layers. (4) Menstrual phase which is due to degeneration, necrosis, and rupture of vessel walls.

Abnormalities of Menstruation.—Although menstruation is normally established in this climate at the age of 12 to 15 years, the age of onset is very variable. In its establishment during the adolescent period, many irregularities occur which are looked upon as functional, due perhaps to deranged or unestablished internal secretions (see Chapter 22). Catamenia normally ceases at about 45 to 50 years of age. At this age, also, there are irregularities, associated with vasomotor disturbances (hot flashes) and with psychic states or neuroses. The menstrual irregularities both of adolescence and the menopause are transient: In youth, regularity of menstruation soon becomes established, and in the fifth or sixth decade menstruation ceases entirely. Symptomatic treatment consists of glandular therapy (oestrin). Should gross and persistent changes *occur, they signify disease.*

Menorrhagia means a menstrual flow (occurring at regular intervals) which is prolonged or profuse or which has an interval of less *than twenty*-eight days. It may be "glandular" or functional in origin (due to too

much estrogen from persisting ovarian follicles or to too little progesterone, the inhibiting hormone of the corpus luteum), but the physician should make a careful examination for *fibroid tumors*, cervical or corporeal polyps, myomas, adenomyomas, and ovarian tumors or *inflammatory disease* of the adnexa (salpingitis, oophoritis, and tuberculosis).

Metrorrhagia means bleeding between menstrual periods. It usually means new growth, *carcinoma of the cervix* or *uterus*, or *polypoid growths in the cervix.*

Dysmenorrhea means painful menstruation, the cause of which often rests on a *neurotic* background.

Amenorrhea means absence of menstruation and usually denotes *pregnancy* or *menopause.* In ectopic pregnancy, where signs may not be clear, the Aschheim-Zondek or Friedman test (rabbit) or Xenopus (frog) test for pregnancy is used but is not always positive. *In order to obtain a positive test for pregnancy, an excess of chorionic gonadotropin must be present in the blood or urine. Since in ectopic pregnancy there may be* a poor development of the trophoblast or the chorionic villi plus a poor connection with maternal tissue, the test is apt to be negative (about 25 to 30 per cent).

Oligomenorrhea means scanty menstruation. It occurs in unmarried women more frequently than in married and is associated with painful breasts. It is normal at the menopause. It is thought to be due to insufficient oestrin hormone and is helped by its administration.

Uterine bleeding may not conform to any abnormal type or combinations such as menometrorrhagia or continuous hemorrhage. *The causes are varied and may include bleeding from* retained gestational products after abortion or full-time delivery and tubal pregnancy, cervicitis with erosion, cervical or corpus carcinoma, systemic causes such as purpura (see Chapter 22).

Every case of abnormal menstruation demands careful bimanual examination, inspection, through the vaginal speculum, smears, and scrapings for cancer cells. If the diagnosis is not positive, diagnostic curettage and cervical biopsy should be done.

Congenital Anomalies

Congenital anomalies may occur in the uterus or vagina. If the Müllerian ducts fail to fuse, a double uterus or double vagina may occur, or there may be an atresia of the cervix or vagina, which prevents the egress of menstrual blood, causing pain and swelling. If the obstruction is at the vaginal orifice, the vagina fills with blood (hematocolpos); also the uterus and the tubes. Other common anomalies are congenital absence of the vagina (and usually with this an absence of the uterus), imperforate hymen, pseudohermaphroditism. Often there are associated anomalies in the kidneys or bladder.

Treatment for a double uterus (bicornis unicollis, didelphys, septatus, arcuatus, etc.) is not often necessary. Complications during pregnancy may require surgery. A double vagina frequently demands a plastic reconstruction. Congenital absence of the vagina necessitates surgery if marriage is contemplated. This is accomplished by bowel transplants, labial grafts, pedicle grafts from the thigh, free split-thickness grafts held in place by a plastic mold, simple pressure against the perineum with a rounded mold over a long period, or simple reconstruction by incision and insertion of a plastic mold until epithelialization occurs. The latter method is easiest and gives fairly good results. Imperforate hymen requires incision. Pseudohermaphroditism is a difficult problem. Adults should be left in the sex in which they have been reared. Gonads should not be removed unless diseased or for diagnosis. The psychological management is important.

Malpositions of the Uterus

We have noted previously that the uterus is held in its normal position by (1) the round ligaments which draw the uterus forward, especially after it has been displaced backward by bladder distention or by pregnancy; (2) the uterosacral ligaments which are part of the endopelvic fascia lying beneath the peritoneum and entering from the cervix to the sacrum—they hold the cervix back and aid in holding it up; (3) the bases of the broad ligaments (cardinal ligaments, ligamentum transversalis colli, Mackenrodt) which are part of the endopelvic fascia and are attached to the intra-abdominal portion of the uterine cervix and the lateral pelvic wall; (4) the fascia *lying between the anterior vaginal wall* and the bladder (subvesical fascia or pubovesical fascia) stretching from the symphysis pubes beneath the bladder to the anterior wall of the cervix; (5) the fascia lying between the posterior vaginal wall and the rectum which is the posterior part of the fascial cylinder encasing the vagina; it is extremely difficult to demonstrate the so-called fascia enumerated in (4) and (5); most authorities now believe that this fascia is really the muscular coat of the vagina; (6) the muscular floor of the pelvis (pubococcygeal fibers of the levator ani muscles). The normal position of the uterus when a woman is standing is approximately horizontal. This position is called one of *anteversion.* Should the entire uterus be tilted backward on an axis at the internal os, it would be in *retroversion.* This is said to be of the first degree when the long axis of the uterus coincides with the long axis of the vagina, of the second degree when the cervix points in the direction of the vaginal orifice, and of the third degree when the cervix points anteriorly. *Lateroversion* means a turning of the uterus to the right or to the left. *Flexion* of the uterus means an angulation of the body of the uterus on the cervix; this may be forward *(anteflexion),* backward *(retroflexion),* or lateral *(lateroflexion).* There may also be combinations of versions and flexions and therefore such terms

as *retroversioflexion*, etc. *Prolapse* of the uterus means a permanent descent of the organ toward the vaginal introitus. There is always some degree of prolapse with retroversion. *Procidentia* means extreme prolapse in which the cervix protrudes from the vaginal orifice. *Complete procidentia* denotes extrusion of the entire uterus from the vaginal orifice. *Torsion* of the uterus means a twisting of the body on the cervix in the vertical axis. *Inversion* means the turning inside out of the entire organ. This is extremely rare.

Most of these conditions are intimately related to the effects of childbirth, although malpositions may be congenital or acquired due to congenital weakness such as procidentia in the nulliparous woman. The uterus is normally held in position by its ligaments and by the pelvic musculature below. Should these structures become relaxed, or should the uterus change its position due to an increase in size or weight, or

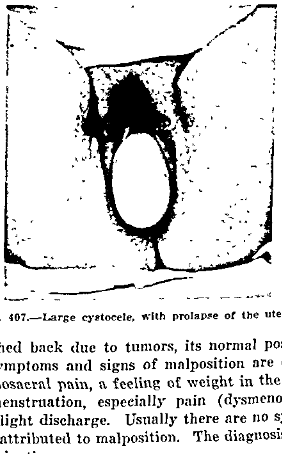

Fig. 407.—Large cystocele, with prolapse of the uterus.

should it be pushed back due to tumors, its normal position would be changed. The symptoms and signs of malposition are of reflex origin and include lumbosacral pain, a feeling of weight in the pelvis, and abnormalities in menstruation, especially pain (dysmenorrhea). Sometimes there is a slight discharge. Usually there are no symptoms which can be definitely attributed to malposition. The diagnosis is easily made by bimanual examination.

The prevention of malpositions may be briefly summarized in the phrase "good obstetrical care." In the minor degrees of retroversion, treatment is unnecessary. In the major degrees with marked symptoms, and in procidentia, surgical treatment is indicated. Many procedures have been devised. In younger women of childbearing age these consist of suspensions by the round ligaments in various manners and the repair of the pelvic floor from below (q.v.). Women with associated organic

lesions require hysterectomy. Older women who are no longer of childbearing age and younger women with complete procidentia demand fixation of the uterus to the anterior abdominal wall, or parametrial fixation. (Vaginal hysterectomy and plastic repair are advised by some.) Childbearing is impossible after this operation, and therefore in the latter group sterilization by salpingectomy is necessary. These operations are also combined with perineal repair. In severe or recurrent cases, complete closure of the vagina (colpocleisis—Le Fort operation) may be indicated. Palliative measures, such as pessaries and tampons, are used where operation is contraindicated.

It is beyond the province of this book to describe each surgical procedure in detail. This information may be obtained from the many excellent textbooks on operative gynecology. However, the number and variety of operations is good evidence that no one form of repair is applicable to all cases and that none are entirely satisfactory. In general they may be grouped as follows:

1. Operations which seek to restore normal position without interfering with the childbearing function by repairing normal structures (plication of round ligaments, drawing them out through the inguinal canal or fastening them to each other in front of the rectus muscles or behind uterus—Olshausen, Alexander, Gilliom, Baldy Webster, etc.; plication of uterosacrals; repair of perineum).

2. Procedures which retain the uterus to act as a supporting structure without retaining its childbearing function (fixation to anterior abdominal wall, interposition or transposition of the uterus under the bladder—ventral fixation; Watkins, etc.).

3. Operations which preserve the uterus but which eliminate the cervix and permit shortening of the cardinal ligaments—Manchester, Fothergill.

4. Excision of the uterus with preservation of the cervix and anchorage of this structure to the round ligaments or anterior abdominal wall.

5. Excision of the uterus and cervix by vaginal hysterectomy and approximation of the round and broad ligaments and reconstruction of pelvic floor.

6. Obliteration of the vaginal canal so that descensus cannot occur. (Le Forte colpocleisis). The particular type of procedure will depend upon: (1) the age and general physical condition of the patient; (2) the desirability of preserving functions—(a) menstruation, (b) childbearing, (c) sexual; (3) The condition of the cervix and corpus uteri; (4) The presence of associated conditions—(a) cystocele, (b) rectocele or enterocele; (5) The degree of descensus.

Infections

One of the most common infections seen in the female genital tract is gonorrhea. This disease is caused by the gonococcus *(Neisseria gonorrhoeae)* and is acquired by contact If affects mucous membranes and

therefore may involve the vulva and vagina (vulvitis and vaginitis), the urethra (urethritis), Skene's glands or the paraurethral glands (skenitis), Bartholin's glands (bartholinitis), the endocervix (endocervicitis), the endosalpinx (salpingitis), the ovaries (ovaritis), and the pelvic peritoneum (pelvic peritonitis). It may also involve the eyes (conjunctivitis) in the newborn or in the adult as a result of carelessness. In children, gonorrhea takes the form of a vulvitis or vaginitis. Children acquire the disease through uncleanliness on the part of adults who are afflicted; adults acquire it by sexual contact. The chief symptoms and signs are a purulent discharge, pain and burning on urination, and, if the tubes and ovaries are involved, pelvic pain, fever, distention, and abdominal muscle rigidity. Bimanual examination reveals fullness in the fornices or the cul-de-sac, fixation of the uterus, and extreme tenderness. Rarely, the infection invades the blood stream, causing gonorrheal arthritis and even endocarditis. The diagnosis is made by urethral and cervical smears which show the gram-negative, intracellular diplococci. The *treatment* consists of bed rest and application of heat locally. The Elliott treatment is the application of intravaginal heat by means of a rubber bag with two tubes through which hot water is allowed to enter and exit. In addition, penicillin is given intramuscularly with sulfonamides by mouth. Formerly, extensive pelvic operations were done in cases with salpingitis and tubo-ovarian abscess. Today, conservative management is the rule. Should an abscess form, it may be drained through the posterior cul-de-sac. Residual tuboovarian abscess may require surgery.

Tuberculosis may involve the tubes and ovaries, causing a tuberculous salpingitis and peritonitis. About 7 per cent of all pelvic infections requiring surgery are said to be due to tuberculosis. Pelvic tuberculosis is usually secondary to infection in the lungs, intestinal tract, or lymph nodes. Skene's glands, Bartholin's glands, the vagina, and cervix are rarely involved. The Fallopian tubes are involved in almost every case of pelvic tuberculosis, the endometrium in about one-half the cases, and the ovaries in about 33 per cent (see Chapter 8). The diagnosis is made from a history of contact and from signs of tuberculosis elsewhere. The local symptoms and signs resemble those of a mild gonorrheal salpingitis. The treatment is, first, the general care of the tuberculosis supplemented with streptomycin in doses up to 1½ Gm. per day. Later, operation may be performed with removal of the diseased tubes. The surgeon must use extreme gentleness to avoid tuberculous fistulae of the intestines. No drainage is employed because secondary infection is feared.

Nonspecific infections are common in the cervix after childbirth. This condition is known as a *cervicitis* or *endocervicitis*. It gives rise to an annoying discharge of a semipurulent character. Treatment is directed at the cause; namely, small, infected cervical tears. Cauterization destroys the infected tissue and the compound racemose glands of the cervix.

Another type of infection is acute and is caused by the *streptococcus*. It occurs after induced abortions and (rarely, now) after delivery. This

dangerous infection spreads to the tubes, ovaries, broad ligaments, and pelvic cellular tissue, causing *parametritis* and *pelvic peritonitis*. Septic emboli may be released from the thrombosed veins of the broad ligaments, causing a septicopyemia and death. Treatment consists of bed rest, ample fluids, repeated blood transfusions, penicillin, the sulfonamides, and *no* surgery unless a localized abscess forms.

Other infections in the cervix are *syphilis, granuloma pyogenicum* and rarely *granuloma inguinale* (Chapter 7). Parasitic infestations are common. *Trichomonas vaginalis* is a parasite which may cause an annoying vaginitis with frothy irritating discharge and pruritus vulvae. The best treatment is careful cleansing and carbarsone or Devegan locally. *Monilia infection* produces a "cheesy" exudate and intense pruritus. It responds quickly to 3 per cent aqueous solution of gentian violet. Actinomycosis and bilharziasis have been reported. *Pruritus vulvae* or persistent itching about the vulva is a common complaint. The cause may be local (trichomonas, vaginalis vaginitis, moniliasis infections, kraurosis vulvae, leucoplakia, senile or atrophic vaginitis, eczema) or general (diabetes, Hodgkin's disease, leucemia, severe neurosis). Treatment is directed against the cause, and, in addition, symptomatic treatment to relieve the itching. In kraurosis or severe leukoplakia vulvectomy may be necessary. "Senile" vaginitis responds well to the estrogens.

Injuries Due to Childbirth

We have seen that malpositions of the uterus may occur following delivery due to relaxation of the supporting structures. We must not infer that every woman will have such changes after the birth of her baby. Nor are *injuries* during childbirth by any means invariable. As the cervix uteri stretches to permit extrusion of the fetal head, small lacerations occur. These are usually inconsequential and heal spontaneously. Large *lacerations* of the cervix may occur under the following conditions: (1) disproportionately large fetal head, (2) precipitate labor, (3) instrumentation. The alert obstetrician will repair these immediately after delivery so that they may heal. If this is not done, they fill in with granulation tissue, and healing by second intention may occur. Frequently, however, they remain as infected, unhealed areas of granulation tissue which protrude into the vagina as an everted red granular mass, commonly called an erosion as distinguished from an ulcer which occurs away from the endocervix with more or less normal epithelium between the ulcer and the external os. The latter are thought to be associated with carcinoma more commonly than the former. In an erosion the surface epithelium is destroyed and the glands are hypertrophied and hyperplastic and secrete a copious amount of mucus. The surrounding tissue is usually edematous and cystic (Nabothian cysts) but may be sclerotic. Inflammatory cells are present in large numbers, and there is a change of the columnar and glandular epithelium to stratified squamous type produced locally from

basal cells and known as *squamous metaplasia*. This process is also seen in respiratory and other epithelium where a "protective" mechanism is invoked by the surface epithelium, changing it to the stratified type. The lesion resembles and must be differentiated from carcinoma, a distinction not always easy since the basement membrane may be intact and only an occasional cell may show loss of polarity and variation in size, shape, and staining quality—"carcinoma in situ." *The lesion causes a profuse* vaginal discharge, which is annoying. Furthermore, carcinoma *may arise* in such areas of chronic ulceration if they are left untreated. Biopsy must be done. The infected areas are excised and sutured (trachelorrhaphy), or, if they are small, *cauterization of the cervix* is done. *The* uterine cervix is frequently obstructed, giving rise to many symptoms such as dysmenorrhea, delayed menses, prolonged bleeding, leucorrhea, infertility. *There may ensue hematomelia, hematosalpinx, pyometra*,

Fig. 408.—Combined rectovaginal and vesicovaginal fistulae. This was in a woman aged 29 years who had had a septic abortion. Subsequently she began to have a temperature up to 105° F. About three weeks after entrance into the hospital it was noted that following an enema the water returned through the vagina. Also the patient complained that there was a constant drainage of urine from the vagina. The diagnosis was a vesicovaginal and rectovaginal fistula, due to gangrenous vaginitis following streptococcic infection induced by septic abortion. The patient had twelve attempts at surgical repair of the fistulae in various hospitals. None of them were successful. In addition to direct attacks upon the fistulous tracts, a panhysterectomy was done and finally a colostomy was established. As a last resort to bring relief to the unfortunate woman, a colpectomy was performed as illustrated in the diagrams. *A*, The condition prior to operations. *B*, The final result. This shows the completed obliteration of the vaginal canal and the bladder draining its contents into the bowel. (Case of Dr. Carl Habich.)

endometriosis as a result of the damming back of menstrual flow. *The* causes are congenital atresia, infections (*vaginitis, cervicitis, syphilis*), *trauma* (*postdelivery, abortion, instrumentation*, cauterization which is followed by dilation, conization, amputation, trachelorrhaphy, hysterotomy, caustic medicaments, foreign bodies), radium and x-ray, neoplasms (carcinoma of cervix or carpus, myomas), senile contracture. *The treatment* depends on the cause.

The perineum is frequently torn or lacerated, especially in primiparas. Anticipating this, most obstetricians perform *an* episiotomy and

then suture the incision after delivery. The purpose is twofold: (1) the wound is an *incised* instead of a *lacerated* one; (2) the extent and direction of the wound is controlled. Lacerations of the perineum may extend to the sphincter ani (incomplete) or into it (complete). In any event, these must be carefully repaired by the obstetrician immediately after delivery. Relaxations or incomplete repairs of the perineum allow the rectum to bulge forward into the vagina, causing a *rectocele.* An overstretching of the fascial layer between the bladder and the vaginal wall *permits the bladder to herniate into the vagina,* causing a *cystocele.* Both conditions may produce annoying symptoms. A cystocele is often accompanied by urgency, frequency, and sometimes incontinence. A rectocele interferes with defecation, causing a bulging, with pain and incomplete evacuation. The treatment consists of restoring the normal position of the uterus (since malposition is usually a causative factor), repair of the anterior vaginal wall (anterior colporrhaphy), and repair of the torn levator ani muscle (perineorrhaphy) and of the posterior vaginal wall (posterior colporrhaphy). These operations must be accompanied by normal placement and fixation of the uterus. Rarely, as a result of injudicious forceps deliveries, horrible tears occur, extending into the bladder. This accident, if not recognized and repaired immediately, results in a *vesicovaginal fistula.* (This is also seen as a result of carcinoma or prolonged radium implantation.) The symptoms of this annoying condition are constant dribbling of urine through the vagina and excoriation about the vulva. The *treatment* consists in carefully denuding the fistulous tract of its lining epithelium and then suturing the bladder and vagina separately by inversion sutures. A catheter is usually placed in the bladder through the urethra and anchored so that there will be no retention of urine. In addition, some surgeons prefer that the patient be kept in the prone position for about one week. In difficult cases the fistula may be closed through a transvesical approach. If all methods fail, ureteral-intestinal anastomosis may be indicated.

Complicated Pregnancy

Ectopic pregnancy refers to pregnancy outside the uterus (extrauterine). The ovum may become implanted in the tube, in the ovary, or in the abdominal cavity. If it becomes implanted in the uterine end of the tube, it is known as **interstitial pregnancy.** After the ovum leaves the ovary it begins its journey into the fimbriated end of the tube and downward into the uterus. Impregnation occurs normally in the tube and then the fertilized ovum continues into the uterus. Should this passage be obstructed because of inflammation or constriction, the fertilized ovum would be arrested at this point and begin its development. The more common causes for such obstructions are gonorrheal salpingitis, puerperal and tuberculous infections of the tubes and ovaries, and congenital malformations.

Normally the ovum grows in the uterine cavity. The uterus is capable of sufficient enlargement to accommodate the fetus until term. When a fertilized ovum is implanted in the tube, it is sure to be destroyed. Under growth, the tubal wall stretches and finally ruptures (tubal rupture), allowing blood and fetal contents to spill into the peritoneal cavity. More commonly, just the fetal capsule ruptures (tubal abortion), and the blood spills into the tube, causing a hematosalpinx.

The symptoms and signs during the first six weeks are those of early pregnancy, with slight enlargement of the uterus. When rupture occurs, there is sudden, severe abdominal pain, with signs of shock, and a slight vaginal bleeding. Cullen's sign is a discoloration about the navel. Although the color is usually blue or greenish-yellow, other colors (red, purple, tan) have been reported. It is not pathognomonic of ectopic pregnancy since it may appear in intra-abdominal bleeding from any cause and also in acute hemorrhagic pancreatitis or any disease causing bloody exudate. Discoloration may occur on the abdomen in such cases not only about the umbilicus, but also in surgical scars, at the sites of perforating vessels, and over hernias. Rarely, a decidual cast is sloughed. Bimanual examination reveals a soft swelling (blood) in the pouch of Douglas or in one fornix. The Friedman test is usually, but not always, positive.

The treatment is immediate operation and removal of the ruptured and bleeding tube. Preparations for transfusion are made and this is given during the operation. Should shock be extreme, operation is impossible, and if transfusions do not bring about a reaction, the surgeon must wait for one. This frequently occurs after a short time and is accomplished by using several veins at once and transfusing under positive pressure. By referring to Chapter 14, the student will see that the three maxims expressed are obeyed in the treatment of ectopic pregnancy. The first one is "treat the patient for shock first;" the second, "never operate in profound shock;" and the third, "there is no operation that has merit enough to be used on a patient who cannot possibly stand it."

Abdominal pregnancy requires long and watchful care. The surgeon *waits* for the fetus to die (this usually occurs later than in tubal pregnancy but rarely does the fetus reach the stage of viability, and if it does it is usually malformed) and for thrombosis of the placental veins to occur. (The placenta is of fetal origin and may be attached anywhere. There is no direct communication between mother and fetus, but in intrauterine pregnancy, infections and toxins may spread to the placenta through the uterine wall.) Operation is performed, the fetus and membranes are removed, and, if the placenta is attached to a tube, ovary, or the omentum, it may also be removed. If attached to a solid organ, removal is impossible because of hemorrhage. In this instance, it is left in situ and the abdomen is closed without drainage.

Cesarean Section.—The surgeon may be called upon to deliver a baby through an abdominal *section*. The indications for this procedure are few but vary with different surgeons. In general, it is indicated when the *life of the mother is endangered*—certain abnormal positions of the fetus with contracted pelvis in the mother, or a great disproportion between the size of the baby and the birth canal, making normal delivery impossible, placenta praevia centralis, and previous section (because of possible rupture of the uterus). Preparations are made for laparotomy and, in addition, for care of the infant. The abdomen is opened through a low midline or oblique incision; then the uterus is opened and the baby delivered. The placenta is next removed and the uterus and abdomen are closed. Three methods are available for Cesarean section: (1) classical method—intestines packed away, uterus opened by longitudinal incision, and then closed by three tiers of sutures; (2) the low-segment or low-cervical method employs a transverse incision of the peritoneum at the uterovesical junction and then a longitudinal (or transverse) incision in the uterus. Closure of the peritoneal flaps gives added security against rupture and postoperative adhesions; (3) extraperitoneal method uses an incision in the paravesical fascia, pushing the bladder down, the peritoneum is stripped upward from the lower uterine segment, and then the uterus is entered through a curved incision. If the peritoneum is inadvertently torn, it is closed before the uterus is opened. This is the safest operation in potentially contaminated cases.

Neoplasms

New growths occur in the female generative organs more commonly than anywhere in the body. New growths of the ovaries have been discussed in Chapter 22.

Solid growths of the ovary are rare (Chapter 22). *Cystic growths* are very common. *Dermoids* containing hair and teeth fragments have already been mentioned. *Teratomas* are not uncommon. These are to be expected in the ovary or testis, for here are the most pluripotent cells of the body—cells from which, in fact, the entire body is derived. The large *pseudomucinous cystadenomas* are usually unilateral and tend to be benign. Rarely, they rupture and cause a pseudomyxoma peritonei, in which the entire peritoneal cavity becomes filled with a jellylike substance. The *serous cystadenomas* are bilateral and may become malignant because of the proliferating papillary outgrowths within their lumen (invertans). These outgrowths finally come through the wall of the cyst (evertans) and are transplanted over the entire peritoneal cavity (proliferating papillary cystadenocarcinoma), causing death.

Endometriosis is the presence of endometrial tissue in abnormal location. The condition is said to be due to a reflux of endometrial cells from the uterus into the tubes during menstruation or a metaplasia of mesodermal tissue or proliferation of congenitally misplaced Müllerian

duct tissues. The term endometriosis interna or adenomyosis (adenomyoma) refers to the lesion in the wall of the uterus and endometriosis externa when it involves other tissues (bowel wall, ovary, tubes, pelvic peritoneum, abdominal wall, bladder, ureters, umbilicus, vagina, vulva, cervix, abdominal and mediastinal lymph nodes, rarely the linings). If large, the lesions are removed and castration is done either by x-ray or bilateral oophorectomy. Small areas regress after castration.

Fig. 469.—Cysts of the ovary. *A.* Dermoid cyst of the ovary showing epithelium and sebaceous glands. *B.* Serous cystadenoma of the ovary. The cyst was filled with clear fluid. Note the deep-staining cuboidal cells which line the cavity. *C.* Pseudomucinous cystadenoma of the ovary. Note the columnar cells which surround the cavities containing pseudomucin. *D.* Corpus luteum cyst of the ovary. Note the crenated edge and the large luteal cells.

Some cysts contain blood (Sampson's cysts, or chocolate cysts). These are due to the presence in the ovary of congenitally misplaced endometrial cells, which bleed with each menstruation, filling the cysts with blood. If the cells migrate into the pouch of Douglas or anywhere else in the pelvis, the same phenomenon occurs (endometriosis), giving rise at times to bizarre symptoms, *made worse at menstruation.* Rarely, such cells are transplanted during an operation into the abdominal

wound. Should these cells survive and ovarian function remain, they, too, would bleed periodically. Bleeding from the umbilicus in infants is usually due to a patent omphalomesenteric (vitelline) duct containing aberrant gastric mucous membrane on which forms peptic ulcer. Rarely this type of bleeding occurs in an adult in whom the condition has been present since birth. In women during the menstrual period, bleeding may occur from endometriosis (the aberrant implantation of edometrial cells).

Still rarer growths of the ovary are the *theca-cell* and *granulosa-cell tumors* which cause a marked change in the secondary sex characteristics, causing young girls to mature at any early age and old women to regain a primitive menstrual function. Also in this group of rarer growths are the *arrhenoblastomas* and the *embryomas* (see Chapter 22).

The physician may suspect the exact type of ovarian lesion present. As a rule, he will make the diagnosis of a solid or cystic ovarian tumor by bimanual examination. Such a finding warrants abdominal operation and the removal of the diseased ovary. Should the cyst be small, it may become twisted on its pedicle, thereby interfering with the ovarian blood supply and demanding an emergency operation because of pain and the possibility of its rupture.

The *Fallopian tubes* and uterine ligaments rarely contain neoplasms. The following varieties have been reported: (1) from epithelium—carcinoma occurring as a primary growth in about 0.25 per cent of all primary malignant growths of the female genital tract; secondary carcinoma may occur from ovarian or uterine carcinomas; (2) from embryonic elements—hydatids of Morgagni (dilated blind ends of Gartner's ducts), para-ovarian cysts (Gartner's ducts dilated and covered with Fallopian tube); (3) from connective tissue—fibroma; (4) from muscle—myoma; (5) from muscle and fibrous tissue—fibromyoma; (6) mesenchymal tissues sarcoma; (7) from chorionic elements—chorioepithelioma; (8) from reticulum cells—plasmacytoma; (9) from endometrium—endometrioma. New Growths of the tubes produce vaginal discharge, pelvic pain, and a tumor. The diagnosis is rarely made with accuracy prior to operation. Surgery consists of bilateral salpingo-oophorectomy with panhysterectomy.

The Uterus and Cervix.—Benign growths such as *polypi*, which are grapelike adenomas of the cervix, are common. They manifest themselves by intermenstrual bleeding. *Papillomas* are occasionally seen near the vaginal orifice. The *urethral caruncle* is a red, pouting tumor (mucous polyp) of the urethra, which causes pain on urination, frequency, and urgency. *Fibromyomas of the uterus* (fibroids) are extremely common. They are multiple and may be intramural, subserous, or submucous; that is, they may be beneath the peritoneal coat, where they cause few or no symptoms except for peritoneal reaction they may excite or symptoms due to their large size, they may lie between the muscle layers of the

uterus, causing its enlargement, or they may be beneath the endometrium, causing engorgement and prolonged menstruation (*menorrhagia*). *Rarely, a fibromyoma may be seen in the inguinal region. Its occurrence here is due to the fact that the gubernaculum of Hunter (analogue of the gubernaculum testis which causes the descent of the ovary) is attached in the inguinal canal. It fuses with the Müllerian* duct of each side in its upper third *and at a point just below its union* with the uterus. It contains muscle fibers *like the uterus and may there*fore develop a fibromyoma. In addition to the benign solid growths, there are many cysts, such as Bartholin's cysts, mucous cysts of the vagina, Nabothian cysts of the cervix, and follicular, dermoid, and luteal cysts of the ovary. The treatment for these conditions is surgical excision through the vagina if accessible (as in the case of a cervical polyp, urethral caruncle, vaginal cyst, or cervical cyst); if not, then abdominal operation must be done. *Multiple fibromyomas* may require the removal *of the uterus (supravaginal hysterectomy). Single tumors may be enucleated (myomectomy). The fibrous tissue may preponderate, and, if so,* it is not affected by the involutional changes at the menopause or the enlargement in pregnancy, whereas the muscle component will stretch in the latter and atrophy in the former instance. Retention cysts of the ovary require either no treatment or simple puncture, whereas dermoids and cystadenomas require the removal of the affected ovary (oophorectomy).

Far more serious are the malignant growths because *of their tendency to spread to adjacent tissues and to metastasize to distant ones. Carcinoma of the cervix* usually occurs *in women* past 40 *years.* It is a *painless* growth in its early stage and manifests itself by intermenstrual bleeding (metrorrhagia) and a foul, dark brown discharge. Since these complaints are not uncommon during the menopause, the patient is apt to overlook their importance. The physician will make a vaginal examination with the use of the speculum and make smears for cell study by the Papanicolaou method or other methods and, *if in doubt, he will take tissue for pathological study.*

Prevention of Carcinoma of the Cervix: Recent studies indicate that "intraepithelial carcinoma" or "carcinoma in situ" is a far more common lesion than formerly suspected. The relationship of carcinoma of the cervix to such diseases as chronic cervicitis and chronic cystic cervicitis, cervical stenosis, cervical empyema, cervical polyps, and cervical granuloma while not proved is strongly suspected. Therefore, *such conditions must be "cleaned up" by cauterization or surgery. A debatable issue is the practice of performing a total* hysterectomy because of the possibility of carcinoma in the remaining cervical stump of the supravaginal hysterectomy. Some statistics show this incidence to be as high as 5 per cent. The performance of a total or panhysterectomy because the remaining cervix might become cancerous is hardly justifiable since *supravaginal* hysterectomy is a much *safer procedure in the average surgeon's hands*

as to morbidity and even mortality. However, if there is cervical disease, the more radical operation is indicated.

Treatment of Carcinoma of Cervix: Because of its early involvement of the ureters, bladder, the broad ligaments, the iliac glands, and the posterior cul-de-sac, excision even by the Wertheim panhysterectomy (removal of the entire uterus, including the cervix, the tubes, the ovaries, and the anatomic lymph glands) often fails to effectuate a cure. Therefore, radium inserted into the cervix and x-ray to the pelvis are the treatment of choice in most cases. This statement is true because of the stage of involvement. The classification usually employed is that of the League of Nations, Radiological subcommittee: stage I, the lesions are confined to the cervix; stage II, there is moderate local invasion; stage III, there is extensive local invasion or unilateral fixation; stage IV, there is great local invasion or metastasis elsewhere. Admittedly it is difficult to establish the exact stage preoperatively because often what appears to be stage I or II in a young healthy person may have lateral involvement on exploration. The largest group are in stage III and the next largest are in stage IV, and for these, radium and x-ray will probably provide the largest number of cures. The effect of radiation may be studied by examining the exfoliated cells in the vaginal smear, and based upon their change, the effect of treatment and the prognosis may be more or less accurately judged. When radium and x-ray are properly employed, the effects on the ureters and bladder are minimal in stage I and II growths. It is true that stage I and II growths are best treated by radical surgery followed by x-ray treatment. Palliative surgery may include urethral transplantation, and heroic efforts to effect a cure may involve, in addition, cystectomy, panhysterectomy, and abdominoperineal resection of the rectum which may also include the vagina. Such measures rarely halt the progress of the disease.

Recently there has been a return to radical surgery, that is, the Wertheim type of operation, especially in stage I and II lesions. Briefly the operation proceeds as follows: (1) ligation and division of the infundibulopelvic and round ligament far from the uterus; (2) incision of the broad ligaments laterally and extending the incision anteriorly through the uterovesical peritoneum and posteriorly to the uterosacral ligaments; (3) dissection of the ureters down to the uterine arteries; (4) separation of bladder from the uterus and vagina; (5) farther dissection of ureters to the bladder; (6) Freeing the uterine arteries which cross the ureters at about the level of the internal os (closest point of the ureters to the uterus is at level of lowermost cervix and here it is about 1 to 1.5 cm.); (7) ligation and division of uterine arteries; (8) ligation and division of uterosacral ligaments; (9) excision of lateral pelvic cellular tissues (Mackenrodt's ligaments and musculofascial sheaths are tied and divided; the bladder may be injured in this dissection unless extreme care is exercised); (10) dissection of vagina down as far as possible; (11) vagina incised and upper part removed; (12) closure of vagina and peritonealization.

Carcinoma of the uterus is less malignant and metastasizes late. It is usually an adenocarcinoma; however, "embryonal" or undifferentiated carcinoma is also found. The interesting adenoacanthoma which is

a metaplasia-like tumor illustrating a squamous-cell change as described in lesions of the cervix (erosions) is also seen. It also occurs after 40 years as a rule. Its chief symptoms are hemorrhage (menorrhagia and metrorrhagia) and a foul, dark discharge. Diagnosis is made by bimanual examination (which reveals uterine enlargement) and search for exfoliated cancer cells in vaginal smears and is confirmed by a *diagnostic curettage* with careful examination of the endometrial scrapings. The treatment is removal of the uterus, the tubes, and the ovaries; that is, panhysterectomy and bilateral salpingo-oophorectomy. Some observers recommend preliminary radiation; others prefer postoperative x-ray therapy and a few employ both pre- and postoperative therapy. Surgery alone, if adequate, gives the best results in early cases, whereas surgery followed by x-ray therapy is the treatment of choice in late cases.

Stilbestrol and excessive estrogenic hormone therapy may induce endometrial hyperplasia and metaplasia. The symptoms (menorrhagia and metrorrhagia) resemble those of carcinoma.

Hydatidiform mole, or cystic degeneration of the chorionic villi, takes place in the placenta (which is of fetal origin), especially in the syncytial cells of the chorion. Several varieties of chorioma have been described. The usual symptom is bleeding after about the fifth month of pregnancy. Diagnosis is made by curettage. The uterus is emptied of its contents, and if the Aschheim-Zondek test remains positive after one to two months, chorioepithelioma is suspected. This demands hysterectomy and x-ray treatment, for it is very malignant, metastasizing by the blood stream and the lymphatics.

Other malignant neoplasms of the uterus include sarcoma (usually spindle or round cells), mixed tumors (teratomas), rhabdomyosarcoma, and chondrosarcoma. *Vulvar carcinoma* represents about 4 per cent of all cancers of the female genital tract. They may be epidermoid carcinoma, melanoma, basal-cell carcinoma, adenocarcinoma (Bartholin gland), vulvar Paget's disease (originating in apocrine glands). Usually they are of the squamous-cell type. Vulvar pruritis, kraurosis, and leucoplakia may be forerunners. The treatment is vulvectomy together with bilateral surgical excision of the inguinal nodes followed by x-ray therapy.

MALE REPRODUCTIVE SYSTEM

Embryology

By referring to the diagram we may see that in the male the Mullerian ducts degenerate, except for a small upper and lower portion (the appendix testis and vagina masculina). The mesonephric duct is functional, its derivatives being the ductus epididymis, the ductus deferens, the ampulla, and the seminal vesicle. The collecting tubules of the mesonephros (wolffian body) form the efferent ductules of the epididymis and the vestigial paradidymis. The phallus enlarges and becomes the penis, into which extends a portion of the urogenital sinus as the urethra. The corpora cavernosa develops from the mesenchyma at seven weeks. The genital tubercle disappears, and the scrotum is developed as a new structure from the labioscrotal swellings, into the vaginal

sacs in which the testes descend. At five months the prepuce is fully developed and covers the glans; at first the adjacent surfaces are fused, but later they again separate except along the undersurface of the glans where the fusion persists as the frenulum.

Anatomy

The male reproductive glands or testes are described in Chapter 22. The duct of each gland, at first very tortuous, forms a structure known as the *epididymis* which lies against the posterior and lateral parts of the testis. The superior part (caput) is attached by many small ducts, and the inferior portion (cauda) by areolar tissue. From the epididymis the excretory duct (ductus deferens) passes upward toward the inferior part of the anterior abdominal wall, which it pierces obliquely (inguinal canal) to enter the abdominal cavity through the internal inguinal ring. Here each ductus deferens is covered by peritoneum and, crossing the pelvic brim, enters the pelvis. The duct then courses along the side wall of the pelvis toward the base of the bladder, where it comes into contact with the *seminal vesicles.* These sacculated structures lie

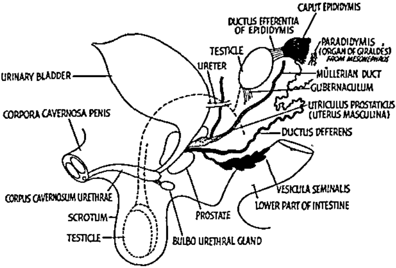

Fig. 410.—Male type of sexual organs. The Müllerian ducts become vestigial, except for the occasional persistence of the lower end as the utriculus prostaticus, or uterus masculina. The Wolffian duct gives rise to the ductus deferens and the seminal vesicles. (Redrawn from Prentiss: Textbook of Embryology.)

between the bladder and rectum and are about two inches long. The duct of the seminal vesicle joins the ductus deferens and forms a short canal called the *ejaculatory duct* which opens into the prostatic part of the urethra. The prostate is a partly glandular, partly muscular structure surrounding the first part of the urethra. The bulbourethral glands (Cowper's glands) lie in relation to the second or membranous portion of the urethra. Their ductules unite to form a single excretory duct which empties into the cavernous portion of the urethra. The ejaculatory ducts empty into the first part of the urethra, opening into a groove on each side of the cresta urethralis. The penis is enclosed by a fascia connected above to Scarpa's fascia and below to the dartos muscle of the scrotum and Colles' fascia. The blood supply to the penis from branches of the internal pudendal artery. The erectile tissue of the corpora cavernosa is supplied chiefly by the deep arteries of the penis, while that of the corpus cavernosum urethral is from the artery to the bulb. The dorsal artery of the penis supplies the erectile tissue and the glans. The veins with which the cavernous spaces communicate carry the blood into the pudendal plexus directly into the dorsal vein and so to the pudendal plexus. The lymph vessels end in the medial nodes of the inguinal group. The nerve supply is from

the hypogastric and pelvic plexuses (to the erectile tissue) and the branches of the pudendal nerve (dorsal nerve of the penis and branches from the perineal nerves). These supply the cutaneous structures.

The prostate is entodermal in origin and develops from the urethral epithelium as multiple outgrowths, which arise above and below the entrance of the male ducts. It varies greatly in size. The average is about 1½ by ¾ by 1¼ inches. The ducts open onto the lateral and posterior walls of the urethra. Glands and ducts of the prostate are embedded in a framework made of fibrous tissue and muscle, and the whole gland is enclosed in a fibrous capsule penetrated by the ejaculatory ducts which open on the verumontanum at about the middle of the prostatic urethra on the posterior side. The ejaculatory ducts run downward medially and forward to open into the prostatic portion of the urethra. The wedge-shaped portion of the prostate which lies between these ducts and the posterior aspect of the urethra is known as the median lobe. When hypertrophied, it causes an elevation and, therefore, partial obstruction to the bladder outlet. The two laterals are not clearly divided but join in front by what has been called an isthmus. The sheath of the prostate is formed by the visceral pelvic fascia and encloses the gland posteriorly and laterally. In the perineal prostatectomy, three potential fascial spaces could be developed between the rectum and prostate: (1) between the muscular wall of the rectum and rectal fascia (posterior layer of Denonvilliers' fascia), (2) between the rectal fascia and anterior layer of Denonvilliers' fascia, and (3) between the anterior layer of Denonvilliers' fascia and the fibromuscular covering of the prostate and seminal vesicles. The prostate receives its blood supply from branches of the hemorrhoidal and inferior vesical arteries. The venous plexus pudendalis surrounds the prostate and reaches the veins of the penis. This plexus communicates with the vesical plexus and draws into the hypogastric veins. The nerves are derived from the hypogastric plexus.

Physiology

The function of the prostate is to aid in reproduction. It has no internal secretion as far as is known. It is an accessory in function along with the seminal vesicle and the bulbourethral glands of Cowper. It often causes obstruction to the bladder outlet because of median bar formations, inflammations, cysts, prostatic calculi, and benign neoplasms, but rarely by cancer.

Congenital Anomalies

The urethra may be double, the second channel emptying into the normal one and lying posterior to it. Congenital strictures may occur, and in children, folds of mucous membrane (valves) in the prostatic urethra may cause an obstruction. Stenosis, atresia, diverticula of the urethra, hypertrophy of the verumontanum, and fistula between the rectum and urethra (Chapter 20) have been reported. The penis may be absent, concealed by the skin of the scrotum, hypoplastic, duplicated (diphallus, *Epispadias* is a dorsal and *hypospadias* a ventral cleft in the male urethra. The latter may occur anywhere along the urethra or in the scrotum. In the perineal type, with bifid scrotum, the genitals may resemble the vulva, although a urethra has never been reported in a clitoris. The treatment of these anomalies is plastic repair. Congenital cysts of the prostate arise from remnants of the Müllerian and wolffian ducts or occlusions of prostatic ducts. Congenital diverticula also occur. Cysts and diverticula should be removed or fulgurated.

Phimosis or congenital narrowing of the prepuce leads to irritation and obstruction. The treatment of this condition is circumcision.

Infections

Infections may occur anywhere along the genitourinary tract. In the penis, nonspecific infections include acute balanitis, cellulitis with or without gangrene, boils, herpes progenitalis, lichen planus, balanitis xerotica obliterans (kraurosis of the penis), and plastic induration (Peyronie's disease). The granulomatous infections which may occur are tuberculosis, syphilis, chancroid, lymphopathia venereum, granuloma inguinale, and histoplasmosis. The urethra is commonly the seat of gonorrheal infection (urethritis), which may extend into the prostate (prostatitis), the seminal vesicles (seminovesiculitis), the epididymis (epididymitis), and the testis (orchitis). This disease is of venereal origin and requires strict quarantine. The treatment is by hypertonic salt packs, the use of penicillin and sulfonamides, and bed rest (q.v.). Instrumentation must not be done. Strictures of the urethra may result, demanding dilatation, or a prostatic abscess may form, requiring drainage in rare instances. So-called nonspecific prostatitis is caused by direct invasion or organisms from the posterior urethra as a rule. The bacteria most frequently encountered are gonococci, staphylococci, streptococci, pneumococci, colon bacilli, and diphtheroids.

Granulomatous infections include tuberculosis, syphilis, actinomycosis, coccidioidomycosis (caused by) *Coccidioides immitis*), and granulomatous prostatitis.

Tuberculosis may affect the epididymides, testicles, seminal vesicles, and, rarely, the prostate. The treatment is, as a rule, conservative. If primary (in the epididymis or seminal vesicles), their removal may halt the spread of the disease.

New Growths

The *prostate* gland is frequently affected by new growth. The various components of the prostate gland may give rise to the following neoplasms: from the epithelium, benign hypertrophy and carcinoma; from connective tissue, fibroma, myxoma, fibrosarcoma, and myxosarcoma; from muscle tissue, leiomyoma, leiomyosarcoma, and rhabdomyosarcoma; from blood vessels, hemangioma and hemangiosarcoma; from lymphoid tissue, lymphoblastoma; from nerves, neurofibroma and neurofibrosarcoma; and from mesodermal elements, chondroma and chondrosarcoma; metastatic tumors also occur. A common type is *diffuse adenosis,* also known as *prostatism* or *adenoma of the prostate,* nodular hyperplasia, fibroglandular hyperplasia, benign hyperplasia. Simple hypertrophy of the prostate also occurs after the fifth decade and is thought to be associated with glandular dysfunction (testis and pituitary) in very much the same way that the fibroadenoma in the breast of the female may be associated with ovarian dysfunction. At times the pathological process is one of fibrosis,

with no increase in size of the prostate. At other times there is a diffuse enlargement due to nodular hyperplasia or stromal hyperplasia and associated with masses of lymphoid tissue. As the hyperplasia continues, the peripheral portion of the prostate is compressed, *forming a false capsule* made of prostate gland. As a result of pressure or associated spasm of the internal sphincter, obstruction of the *prostatic urethra* occurs and interferes with urination, so that there is a retention of urine, with formation of a small pouch in which the urine accumulates. The symptoms at first are usually nocturnal frequency and dysuria. Sometimes acute retention occurs. If left untreated, infections supervene which may involve the bladder, the ureters, and the kidneys. Diagnosis is made by rectal examination and cystoscopic examination, if possible. The treatment is *transurethral*,

Fig. 411.—Adenomatous hypertrophy of the prostate (benign prostatic hypertrophy). Note the cystic areas, which are due to a dilatation of the acini. There is great infolding of the epithelium into the lumina of the acini. Occasionally such lesions show a hypertrophy of muscle tissue as well as of connective tissue. This patient had urinary obstruction due to the enlarged prostate. The prostate was successfully removed through a suprapubic incision.

partial prostatectomy, which is done through the urethroscope with a cautery loop, or *suprapubic prostatectomy*, which is done through the bladder. The former operation removes the obstructing wedge. The latter attempts to remove the affected portions of the lobes (*lobectomy*), leaving a rim of compressed prostate behind. Other methods are the retropubic and perineal.

Transurethral resection has the lowest mortality and morbidity. However, incomplete removal, distortions and strictures of the urethra and vesical neck, incontinency, and early recurrence of symptoms have limited its use according to some urologists, whereas others find few, if any, contraindications to its use. All are agreed that the procedure is useful for

the removal of bars, median lobes, vesical neck contractures, smaller prostates which protrude into the bladder, and in neurogenic bladder. It is an especially desirable procedure in poor-risk patients, and those with associated pathological changes in the bladder such as papillomas and calculi; also in younger patients the operation is useful because of preservation of sexual function.

Suprapubic prostatic resection is the easiest method to use. It is usually employed in large prostates or those associated with large or inaccessible bladder tumors, large or multiple stones, and diverticula of the bladder. It is not used in fibrotic or calcareous or cancerous obstructions.

Perineal prostatectomy is more difficult but will take care of almost any pathological condition in the gland. It is in connection with this operation as developed by Dr. Hugh Young that early postoperative ambulation was practiced, an especially useful maneuver in older people.

Retropubic prostatectomy is useful in benign hypertrophy of the lateral or median lobes or both and calculous disease of the prostate, especially when associated with benign hypertrophy. The operation is done through a low midline incision. The prevesical space is exposed. The prevesical fat and peritoneal fold are then pushed upward. The endopelvic fascia is incised transversely, an inverted V incision is made in the false capsule, and the enteral lobes are brought up, the pedicles clamped, and the lobes removed. The median lobe is then enucleated from below and behind the floor of the vesical outlet. The bladder neck is incised if it is small, and a Foley balloon catheter is passed up through the urethra through the prostatic cavity into the bladder. The false capsule and endopelvic fascia are then closed.

Carcinoma of the prostate is a common disease and is said to cause 5 per cent of all deaths in men past 50 years of age. Normal development and maintenance of the prostate requires testicular male hormones influenced by gonadotropic hormones secreted by the anterior pituitary. Castration causes simple atrophy of the normal prostate and hyperplasia and increased secretory activity of the anterior pitutiary and perhaps the adrenals. This is not true of the hypertrophied prostate. The normal adult prostate tissue is extremely rich in phosphatose with optimum activity at pH 5.0. Both acid and alkaline phosphatase are capable of dephosphorylating monophosphoric esters to form inorganic phosphate. Alkaline phosphatase is present in large amount in osteoblasts, and therefore when there is prodigious osteoblastic activity, this enzyme is increased—rapid growth in children, Paget's disease of bone, osteogenic osteoblastic sarcoma, and osteoblastic metastases from prostatic cancer. In Chapter 22 we learned that alkaline phosphatase is also increased in disease of the liver. *Acid phosphatase is increased only in cancer of the prostate with metastases* to bone or lymph nodes. Here the secretions of metastatic cells find their way into the blood plasma, increasing the acid phosphatase above normal. The normal value (King and Armstrong

method) is less than 4.5 units for acid phosphatase and less than 12.5 units per 100 c.c. of serum for alkaline phosphatase.

Prostatic cancer is either of the undifferentiated or adenocarcinoma type. It rarely ulcerates through the rectovesical fascia into the rectum but often extends into the bladder in the trigone. The spread is also apt to be along the surface of the seminal vesicles and the perineural lymphatics. Bone marrow and lymph nodes are frequently involved but the lungs or brain seldom. Cancer of the prostate has been successfully transplanted heterologously into guinea pigs, and here it is under the influence of endocrine factors as in its primary habitat, but it loses its acid phosphatase activity.

Symptoms and signs are variable and usually insidious. In a man 50 years of age or over who complains of some frequency and difficulty in urination with low backache and scrotic pain and loss of weight, cancer of the prostate should be suspected. The symptoms are usually of a few months' duration. On rectal examination there is a hard lumpy prostate, or a single lump may be present. In late cases there is a diffuse hardness into surrounding tissues.

Carcinoma cells may be found in prostatic secretions, and this should be done routinely in suspected cases. X-ray of the pelvis and spine may reveal osteolytic or osteoblastic lesions. The long bones are not often involved, and very rarely below the elbow or knee. Cystoscopic examination may show infiltration of the trigone or notches around the vesical neck. A study of serum acid phosphatase is diagnostic in the lesions which have already metastasized. Biopsy is sometimes necessary and may be done through the perineum so that perineal prostatectomy may be carried out if the diagnosis is positive. A special stain for acid phosphatase (Gomori) will help differentiate between carcinoma of the prostate and carcinoma of the bladder.

The treatment of cancer of the prostate is surgical removal of the gland by perineal route if the lesion is early. This is not often possible. Antiandrogenic treatment is based on the fact that cancer of the prostate is stimulated by injection of male sex hormone (androgens) and is inhibited by reduction of androgens either through castration or neutralization through the administration of female sex hormones (estrogens). Serum acid phosphatase decreases when diethylstilbestrol, 5 mg. daily, is injected, whereas it increases when testosterone propionate, 25 mg. daily, is given. Great improvement follows administration of estrogens not only in the prostate, but in the metastatic areas as well. Bilateral orchiectomy is the treatment of choice because it is more complete and more permanent than estrogenic therapy. The latter should be used when castration is refused or when the diagnosis is doubtful or if surgery is too risky because of the debility of the patient. Failures occur in both methods due to the androgen-independent quality of the cancer or the production of androgens in the adrenals (see Chapter 22). X-ray treatment is not often successful except insofar as it produces sterilization.

Teratoma of the testicle is described in Chapter 22. New growths of the external genitals also occur. They are Leucoplakia, Paget's disease, Bowen's disease, papilloma (penile horn, condyloma acuminatum). Carcinoma of the penis occurs, as a rule, under the prepuce. Metastasis occurs early to the superficial inguinal glands. The treatment consists of resection of the organ, together with excision of the inguinal glands on either side.

THE URINARY SYSTEM

Embryology

The kidney in its embryological development recapitulates philogeny. The *pronephros* (fore-kidney) is the functional kidney of some of the lowest vertebrates *(Hemichorda)*. It is called the fore-kidney or head kidney because it lies in the animal's proboscis. Here it forms a puckered membrane richly supplied with blood vessels (glomerulus) and appears to act as a kidney. The pronephros contains only two to five straight tubules and is considered a precocious development of the most anterior tubules of the nephrotomes. (See Fig. 412.)

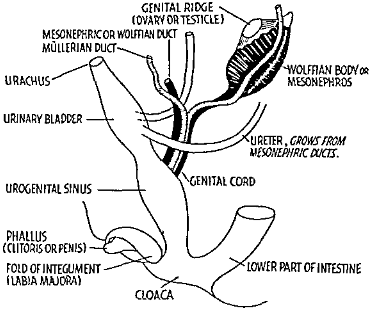

Fig. 412.—Primitive urogenital organs. Embryo of about 6 weeks (up to 12 mm.). This represents the undifferentiated stage. (Redrawn from Allen Thompson, and from Prentiss: Textbook of Embryology.)

The *mesonephros* (mid-kidney or wolffian body) usually forms the functional kidney in adult fishes and amphibians. The tubules are more numerous and more convoluted, and they enter into close connection with the genital organ. In mammals the true or permanent kidneys arise later and the wolffian bodies degenerate, being retained only as a portion of the epididymis in the male and as certain vestigial structures in the female (the parovarium, epoophoron, and paroophoron, and sometimes the cyst of Morgagni).

From the diffuse *substantia cellulosa* along the ventral side of the spinal column, as seen in the chick embryo on the third day of incubation, appear the *wolffian ducts* emptying into the cloaca. Since the wolffian duct is primarily the duct of the anterior kidney or pronephros, it is called the *pronephric duct* by some but is more often

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dependent on the effective pressures which result from such an arrangement. Here, as elsewhere in the body, the osmotic pressure, the hydrostatic pressure, and the permeability of the capillary determine the movement of fluid (see Chapter 11). In the tubules the capillaries are covered by tubular epithelium. If this is destroyed, uncovering the capillaries (as in mercury poisoning), absorption may be greatly increased, resulting in anuria, other factors remaining constant. All of the blood which enters the kidney passes through the glomerular tufts except a small amount which nourishes the capsule and interstitial tissue. Thus the tubules are supplied with blood which has gone through the glomeruli. Very few anastomoses exist between glomerular or tubular vessels, and the afferent components resemble arterioles, whereas the efferent are much smaller in diameter.

The *ureters* are also retroperitoneal. The left ureter descends close to the aorta in front of the common iliac artery; the right descends along the vena cava and in front of the external iliac; both ureters pass behind the uterine arteries and enter the bladder obliquely and somewhat laterally. The abdominal part of the ureter receives its blood supply from the renal and internal spermatic arteries. The pelvic portion is supplied by the superior vesicle and middle hemorrhoidal vessels. The nerves reach the ureter through the renal, spermatic, and hypogastric plexuses.

The *bladder* is covered by peritoneum except for a small space anteriorly, which is accessible only when the bladder is distended. The space of Retzius lies between the bladder and the pubis and contains many veins and loose areolar tissue. This is the uncovered area of the bladder, and cystectomy is performed here. The bladder occupies a much higher position in children than in the adult. Even when empty, it is an abdominal organ. The peritoneum forming the rectovesical pouch covers the whole of the posterior surface of the bladder and reaches as low as the upper limit of the prostate. The internal urethral orifice is high at birth (level of symphysis pubic upper margin) and then sinks to a lower level. The openings of the ureters lie on a plane with the pelvic brim. The obliterated portions of the umbilical arteries lie closer to the bladder than in the adult as they pass upward toward the umbilicus.

The bladder is held in position by the ligamentum umbilicale medium (fibrous cord of the urachus) which binds the apex to the anterior abdominal wall, by the false ligaments which are peritoneal folds (lateral, superior, and posterior) by the connective tissue attachment to the symphysis anteriorly, the lateral loose areolar attachments to the fascial lining, by processes of the pelvic fascia continuous with those forming the sheath of the prostate (puboprostatic or anterior ligaments, reaching the bladder from the pubis in front; lateral ligaments reaching the bladder from the side wall of the pelvis), by fibrous and unstriped muscular tisue which surrounds the seminal vesicles, and by the terminal portions of the ductus deferentes and the ureters.

In the female the basal part of the bladder is supported and held in place by its connections with the anterior wall of the vagina. The region of the urethral orifice is the most firmly fixed part of the bladder in both sexes.

The bladder receives its blood supply bilaterally from the superior vesical arteries (from the umbilicals just before they become obliterated) and the inferior vesical arteries (from the hypogastrics). The veins are found just above the prostate and in the region of the ureter-bladder junction. They form plexuses and empty into the tributaries of the hypogastric veins and communicate below with the pudendal venous plexus.

The lymph vessels drawing the anterior wall follow the obliterated hypogastrics on either side toward the neck of the bladder, near the origin of the ureter. There they turn laterally after receiving trunks from the posterior wall and then join the primary nodes. The posterior bladder wall collectors usually leave the bladder wall separately to course to the nodes of the first echelon; namely, the external iliac nodes and occasionally the hypogastric and common iliac nodes. The nerve supply on each side is

referred to as the *mesonephric duct*. An outgrowth from this duct enters into the formation of the permanent kidney. The duct itself degenerates in the female, leaving only the vestigial Gartner's duct, in which cysts sometimes form; in the male, it is retained as the ductus epididymis, the ductus deferens, and the seminal vesicle.

All the renal organs—the pronephros, the wolffian body (mesonephros), and the kidney (metanephros)—are developed from the nephrotomes. They are all composed of mesodermal tubules, each of which is in close relation with a knot of capillary blood vessels derived from branches of the aorta. Such a knot of vessels is called a *glomerulus*.

The *metanephros* (hind-kidney) is the functional kidney in reptiles, birds, and mammals, arising from a caudal position in man. It develops after the wolffian body has been formed. It arises from two parts: one, an outgrowth of the wolffian duct, forms the ureter, and the pelvis, calyces, and collecting tubules of the kidney; the other, a mass of dense mesenchyma (metanephric cell mass), surrounds this outgrowth and gives rise to the uriniferous tubules, the blind ends of which become invaginated and envelop the glomeruli and are known as Bowman's capsule. The unit is called the Malpighian body or renal corpuscle.

The short functional tubules of the adult kidney lie in the region where these developmentally distinct portions of the kidney unite. These two parts may fail to unite in the same plane. Failure of the two parts to join properly results in congenital cystic dilatations.

Anatomy

The *kidneys* lie behind the peritoneum, the left a little higher than the right, and are crossed by the eleventh and twelfth ribs. The right kidney is in close relation with the duodenum; the left, with the tail of the pancreas, the stomach, and the splenic flexure. Superior to the kidneys are the adrenal glands. The transversalis fascia (fascia renalis) splits to enclose the kidneys. The anterior layer covers the renal vessels, the aorta, and the inferior vena cava and is continuous with the other side. The posterior is attached to the vertebral column. Between the layers is a pad of fat, which also surrounds the kidney. Above, the two layers unite, but below, there is an opening, so that exudates may extend downward on the psoas muscle. The kidney is a compound tubular gland which is roughly divided into two components: (a) secretory, composed of the nephron, and (b) excretory, composed of ducts which convey the urine to the ureter which is the large excretory duct arising in the kidney's hilus and ending in the urinary bladder. The latter is a storage unit which expels the urine to the outside through the urethra. The kidney capsule is made of dense collagenous bundles and some elastic fibers. The glandular part of the kidney surrounds the sinus which contains the renal pelvis and is filled with loose connective tissue and fat vessels and nerves. The pelvis is the funnel-shaped beginning of the ureter. The wide part of the funnel faces the renal tissue and forms several projections known as major calyces, each of which in turn has several outpocketings known as minor calyces. The outer part of the kidney is known as the cortex and it surrounds the medullary substance composed of eight to eighteen renal pyramids (malpighian). These pyramids are cones with their bases pointing peripherally and their apices or *papillae* projecting into the lumen of each minor calyx. The papilla is perforated by ten to twenty-five small openings—the area cribrosa. The renal columns (Bertin) are formed by the dark brown cortex separating the pyramids. The pyramids can be considered as lobes which in the fetal period are separated from each other by connective tissue and which fuse later. Sometimes they remain separate throughout life as they do also in the ox. The pyramids may be subdivided into lobules because of the branching of the excretory ducts.

The kidneys' arterial supply is close to the aorta and therefore its hydrostatic pressure is high. The renal artery breaks up suddenly into short branches within the kidney. This supply is all one vessel so far as each glomerulus is concerned, with its afferent, efferent, and tubular components finally becoming venous. Filtration is largely

cutaneously, carba-minoyl-choline (Doryl). These drugs are contraindicated in vesical neck obstructions, asthma, hyperthyroidism, bowel surgery, in elderly people, and in those with coronary disease. *Reactions* such as dizziness, nausea, flushing, and even vomiting are not uncommon. Prostigmine (1 c.c. of a 1:4000 solution hypodermatically) has been used with success. (b) Parasympathetic depressants—atropine is of little use but, at times, may for unaccountable reasons give good results; the same is true of Syntropan 50 to 100 mg., by mouth. If more than four catheterizations are necessary, a catheter is anchored for a twenty-four-hour period and then removed. This is at variance with most teaching, but an anchored catheter means immobilization in bed and this perpetuates a general as well as a bladder atonic state. During catheterization and for a short time thereafter Sulamyd, 0.5 Gm., is given by mouth every four hours. If nothing is permitted by mouth, penicillin and streptomycin may be given intramuscularly as prophylactics against bladder infection. Ambulation with a catheter in place may be necessary, particularly in male patients who have had bladder surgery. This will not be necessary, as a rule, for other postoperative retention because early mobilization ordinarily precludes urinary retention.

The Paralyzed Bladder.—The term "atonic" bladder is used loosely to describe a bladder which cannot be emptied voluntarily. Tone implies a condition of tension in the detrusor muscle which, when increased, sends impulses to the central nervous system, initiating the "voiding reflex." Atonicity occurs when there has been overdistention for a varying period of time or when there has been an interruption of the segmental reflex concerned with micturition. *Often it is the overdistention* that leads to atony, even in the presence of such conditions as tabes dorsalis (loss of sensation) or spinal injury (loss of entire segmental reflex arc) (see Chapter 18). The treatment of the paralyzed bladder is designed to keep it clean and elastic so that when automaticity sets in, it will be in condition to respond and not become a small contracted infected organ. To accomplish this, the vesical neck should be open (removal of prostatic obstruction or stones), and a closed system of irrigation with a slight pressure gradient should be instituted (Chapter 18). Specific aids include (1) the use of mild antiseptic solutions, (2) "G" and "M" citric acid solutions to dissolve crusts, (3) the use of small Foley catheters (F16 or 18), (4) attention to acid-base, protein and electrolyte balance, (5) frequent trials at urination with cystometric readings to determine pressure and capacity of the bladder, and tests for residual will show the ability of automatic control, (6) Sulamyd as a prophylactic aided by penicillin and streptomycin when infection is present in the epididymis or kidney, (7) early ambulation insofar as possible, (8) attention to bed sores (see Chapter 6), (9) anterior rhizotomy in some cases changes a paralysis from the spastic type with its mass reflex to a flaccid type.

derived from the vesical plexus, the fibers of which come from the upper lumbar nerves through the hypogastric plexus and from the third and fourth sacral nerves, whose fibers join the vesical plexus directly.

Physiology and Functional Derangements of the Urinary Bladder

Postoperative urinary retention is common in spite of the fact that the bladder is full and there is no organic obstruction to account for the inability to void. The urinary bladder normally fills passively and empties under voluntary control. We have seen that the sympathetic nerve supply to the bladder is through the presacral and hypogastric nerves. Stimulation of these nerves relaxes the wall and contracts the internal sphincter. The parasympathetic nerve supply is by way of the nervi erigentes. Stimulation of this nerve causes relaxation of the external sphincter and contraction of the detrusor. Voluntary control of the external sphincter and other perineal accessory muscles is through the pudendal nerve. The desire to void comes from intravesical pressure, usually caused by 250 to 300 c.c. of urine in the adult.

Postoperative urinary retention is due to many factors: (1) psychic (position on voiding, embarrassment, previous experience); (2) pain (contraction of accessory muscles causes this); (3) reflex inhibition due to pain (especially after rectal operations, herniorrhaphy, vaginal operations, interference through pudendal nerves); (4) sedation so that desire is not felt until overdistention occurs; (5) partial paralysis of detrusor (which constitutes the entire bladder mechanism) due to overdistention for long periods; (6) irregularity of urine accumulation, at first very little urine, then a rather sudden large amount, especially after intravenous medication; (7) actual injury to nervi erigentes in abdominoperineal resection; (8) displacement of bladder after certain gynecological operations.

Treatment: Since the advent of early mobilization, the problem of postoperative retention has greatly diminished. Patients are allowed to sit up or stand up as soon as consciousness returns. Should the patient void small amounts frequently, overflow incontinence should be suspected and catheterization done immediately after voiding. Overdistention should be avoided because it leads to atony and actual injury to the bladder wall with small petechial hemorrhages resulting. Residual urine in an atonic bladder leads to cystitis because the urine acts as a good culture medium and the atonic bladder is susceptible to infection. Simple measures and an indifferent attitude by the surgeon should be tried first. Some aids are as follows: Sitting on commode or standing (male). (2) Privacy during urination. (3) Warm packs or water bottle to perineum. (4) Warm retention enema of physiological saline with 60 mg. of procaine or simply warm water as an enema. (5) Drugs—(a) parasympathetic stimulants such as acetyl-beta-methylcholine (Mecholyl chloride) 25 to 50 mg. by mouth, beta-methylcholine urethane, 5 mg. sub-

5. Ureterovaginal fistulae may be congenital or acquired (operative—especially vaginal hysterectomy or irradiation injury). Treatment consists of transplantation of the ureter into the bladder.

Physiology and Functional Derangement of the Kidneys

Physiology.—

The kidney's functional or secretory unit is the nephron, which consists of the renal corpuscle with its Bowman's capsule, the proximal convoluted tubule, the descending and ascending limbs of Henle's loop, and the distal convoluted tubule. A short connecting tube joins the collecting tubule or excretory duct with the nephron. These excretory tubules convey the urine to the ureter. The connections of the collecting tubules with the nephrons are located in the cortex and are called the "peripheral branchings" of the collecting ducts. From here they pass inward and become larger (papillary ducts of Bellini) and open on the area cribrosa, the apex of the papilla. The mode of action of the kidneys has been the object of much research, but even now there are differences of opinion. Certain experiments may be cited. The kidney has been removed and transplanted into the neck of experimental animals by suturing the carotid artery and jugular vein to its vascular pedicle, and, although deprived entirely of its nerve supply, continues to function without nervous control. Secondly, Goldblatt has shown the effect of partial constriction of the renal artery on the blood pressure, demonstrating that a rise is attained by this method, whereas complete ligation of the artery or nephrectomy (unilateral or bilateral) is not accompanied by a similar rise. This has led to the assumption that when the blood supply of the kidney is diminished, a pressor substance is liberated which causes an increase in blood pressure.

Theories of renal function date back to Bowman and Heidenhain. Bowman discovered the relation between the glomeruli and the tubules; Heidenhain thought that the formation of urine was a secretory process. Ludwig believed that the glomerulus acted as a filter and that the walls of the renal tubules acted as absorbing membranes. Cushny believes that absorption by the cells of the tubules is selective. We have already seen in Chapter 11 that the kidney plays an important role in maintaining the level of the body fluids. We have also seen that according to Starling, filtration and absorption are the results, respectively, of hydrostatic and osmotic pressure. Since the hydrostatic pressure in the afferent arteriole of the glomerulus is about 75 mm. Hg and the osmotic pressure is about 30 mm., there is a possible effective filtration pressure of about 45 mm. The pressure in Bowman's capsule is 5 mm., which is, of course, too little to affect filtration. The pressure in the capillary loop is about 60 per cent of the systolic pressure, or about 70 to 80 mm. Hg. Should the systolic blood pressure fall sufficiently to bring the capillary pressure below the osmotic pressure, we should expect urinary suppression to occur, and this actually happens when the pressure in the afferent arteriole falls to a level of 35 to 50 mm. Hg. The injection of isotonic salt solution causes profuse diuresis because it dilutes the plasma and therefore decreases the osmotic pressure. The injection of gum acacia or gelatine does not cause so great a diuresis because these solutions have a higher colloid osmotic pressure. When the blood pressure is extremely low, injection of large amounts of normal saline restores urine formation by diluting the plasma colloids, increasing the blood volume, and so increasing the hydrostatic pressure. Should urine formation cease because the intracapsular pressure in the renal corpuscle exceeded the filtration pressure, it could be restored by diluting the blood with isotonic salt solution, which would lower the colloid osmotic pressure and so increase the effective filtration pressure. The dependence of urine formation on filtration pressure differentiates the kidney from the truly secretory gland, such as the salivary, in which secretion continues for a time in spite of obstruction of the duct.

On the basis of Starling's theory of filtration, it is easy to explain many clinical facts, such as the loss of protein due to damaged capillaries in the nephrotic kidney

Incontinence in Women.—

1. Stress incontinence is a condition occurring in women usually as a result of a urethrocele but sometimes without any visible lesion. It manifests itself by a slight dribble of urine when intra-abdominal pressure is increased (sneezing, coughing, lifting) or, in severe cases, on the slightest motion. The treatment consists of surgical repair of the urethrocele and usually the accompanying cystocele and procidentia. These operations have been discussed previously in this chapter and include advancement operations, advancement with transfer of cardinal ligaments and amputation of the cervix (Manchester or Fothergill operation), transposition operation (Watkins), vaginal hysterectomy, and plastic repair. Special operations for the urethrocele include plication of the urethral sphincter (Kelly), overlapping of supporting pubocervical fascia, and other plastic procedures utilizing residual tissues. In addition, fascial slings have been employed, using the fascia lata of the thigh and the anterior rectus sheath (Goebell-Frangenheim-Stoeckel).

2. Vesicovaginal fistulae have been discussed previously in this chapter. They may be due to childbirth injuries, surgical injuries, malignancy of the vaginal and bladder walls, and irradiation therapy. The treatment is surgical and will vary with the position and size of the fistula. A few general principles concerning the management of this defect should be stressed. (1) Use healthy tissue for suture. This is done by waiting more than six months after discovery of the lesion and then excising all scar or unhealthy tissue. Failure to get union means more scar tissue and as in the repair of cleft palate, each failure makes more uncertain the ultimate success because scar tissue is poor healing material and if completely excised after many trials the defect becomes enormous. If incompletely cut out, the tissue remaining does not heal easily (see Chapter 3). (2) Adequate exposure. This may be facilitated by a lateral episiotomy (Schuchardt). (3) Adequate mobilization of flaps even at the expense of shortening the vagina. This is necessary to avoid tension on the suture line and to afford broad surface opposition. (4) Separation of bladder from vagina. In accomplishing (3) this will usually be done but it should be meticulously complete. (5) Suture of bladder and vagina in opposite direction. (6) Relaxing incision if necessary. (7) Rest to the part by catheter or suprapubic drainage (if fistula is close to urethra). (8) Prone position on Bradford frame.

3. Incontinence may result from urethral and sphincteric defects due to congenital anomalies, violent trauma, obstetrical and surgical accidents, malignancy, and lymphopathia venereum. Treatment consists of attempts at forming a new urethra. First, adequate drainage is obtained through cystotomy. Then vaginal flaps are dissected up, the remaining sphincter region of the bladder is reconstructed with silk sutures, and the vagina mucosa used to cover the newly created sphincter.

4. Neurological disease incontinence (spina bifida, multiple sclerosis, tabes dorsalis, spinal cord injury) has been discussed.

5. Ureterovaginal fistulae may be congenital or acquired (operative—especially vaginal hysterectomy or irradiation injury). Treatment consists of transplantation of the ureter into the bladder.

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The kidney's functional or secretory unit is the nephron, which consists of the renal corpuscle with its Bowman's capsule, the proximal convoluted tubule, the descending and ascending limbs of Henle's loop, and the distal convoluted tubule. A short connecting tube joins the collecting tubule or excretory duct with the nephron. These excretory tubules convey the urine to the ureter. The connections of the collecting tubules with the nephrons are located in the cortex and are called the "peripheral branchings" of the collecting ducts. From here they pass inward and become larger (papillary ducts of Bellini) and open on the area cribrosa, the apex of the papilla. The mode of action of the kidneys has been the object of much research, but even now there are differences of opinion. Certain experiments may be cited. The kidney has been removed and transplanted into the neck of experimental animals by suturing the carotid artery and jugular vein to its vascular pedicle, and, although deprived entirely of its nerve supply, continues to function without nervous control. Secondly, Goldblatt has shown the effect of partial constriction of the renal artery on the blood pressure, demonstrating that a rise is attained by this method, whereas complete ligation of the artery or nephrectomy (unilateral or bilateral) is not accompanied by a similar rise. This has led to the assumption that when the blood supply of the kidney is diminished, a pressor substance is liberated which causes an increase in blood pressure.

Theories of renal function date back to Bowman and Heidenhain. Bowman discovered the relation between the glomeruli and the tubules; Heidenhain thought that the formation of urine was a secretory process. Ludwig believed that the glomerulus acted as a filter and that the walls of the renal tubules acted as absorbing membranes. Cushny believes that absorption by the cells of the tubules is selective. We have already seen in Chapter 11 that the kidney plays an important role in maintaining the level of the body fluids. We have also seen that according to Starling, filtration and absorption are the results, respectively, of hydrostatic and osmotic pressure. Since the hydrostatic pressure in the afferent arteriole of the glomerulus is about 75 mm. Hg and the osmotic pressure is about 30 mm., there is a possible effective filtration pressure of about 45 mm. The pressure in Bowman's capsule is 5 mm., which is, of course, too little to affect filtration. The pressure in the capillary loop is about 60 per cent of the systolic pressure, or about 70 to 80 mm. Hg. Should the systolic blood pressure fall sufficiently to bring the capillary pressure below the osmotic pressure, we should expect urinary suppression to occur, and this actually happens when the pressure in the afferent arteriole falls to a level of 35 to 50 mm. Hg. The injection of isotonic salt solution causes profuse diuresis because it dilutes the plasma and therefore decreases the osmotic pressure. The injection of gum acacia or gelatine does not cause so great a diuresis because these solutions have a higher colloid osmotic pressure. When the blood pressure is extremely low, injection of large amounts of normal saline restores urine formation by diluting the plasma colloids, increasing the blood volume, and so increasing the hydrostatic pressure. Should urine formation cease because the intracapsular pressure in the renal corpuscle exceeded the filtration pressure, it could be restored by diluting the blood with isotonic salt solution, which would lower the colloid osmotic pressure and so increase the effective filtration pressure. The dependence of urine formation on filtration pressure differentiates the kidney from the truly secretory gland, such as the salivary, in which secretion continues for a time in spite of obstruction of the duct.

On the basis of Starling's theory of filtration, it is easy to explain many clinical facts, such as the loss of protein due to damaged capillaries in the nephrotic kidney

or the retention of nitrogen by the capillaries of the sclerotic kidney. Damaged capillaries allow the escape of plasma, deplete the blood protein, and reduce the blood osmotic pressure, with resultant edema. Sclerotic capillaries retain nitrogen while allowing the escape of fluids, producing azotemia and renal insufficiency. It should be remembered, however, that reabsorption in the kidney tubules cannot be explained on purely chemical grounds. Certain substances (such as glucose) are reabsorbed against a gradient; that is, work is done by the kidney cells. The process, in short, is one of selective absorption. The reabsorption of water by the tubules is probably regulated by the antidiuretic hormone of the pituitary (see Chapter 11).

The functions of the kidney, then, include not only filtration and excretion, but also absorption, synthesis (hippuric acid and ammonia), and even secretion by the tubules of certain dyes and creatinine. At least nine-tenths of the volume of "urine" that goes through the glomerulus is absorbed by osmosis. The concentration of this urine is explained by the absorptive action of the tubules.

An important anatomic arrangement which has recently been re-emphasized is the juxtaglomerular apparatus. This is a cuff of neuromyoepithelioid cells more prominent in the wall of the afferent arteriole. That portion of the distal convoluted tubule which lies in contact with this cuff of cells is shown by histological study to differ from neighboring epithelial cells in that the cells covering this area are tall columnar cells which show a peculiar striation in the basilar portion of the cytoplasm. This plaque of epithelium is known as the *macula densa*.

The function of this mechanism is not definitely known. Variations in the concentrations of urine affect it and thereby regulate the volume of blood entering the glomerulus. The mechanism resembles the shunt in the glomus of the skin.

The kidneys are the buffer organs for fluid excretion and waste excretion, and they share with the lungs acid-base regulation (Chapter 12). The afferent arteriole enters the glomerulus, carries blood to the glomerular capillaries for the elaboration of a glomerular filtrate, becomes efferent after leaving the glomerulus, and continues in intimate contact with the convoluted tubules through a second capillary network, and, then, after the functions of excretion and reabsorption are performed, it becomes a venule.

Apparently the kidney does not work in units—it is all or none (*Talbott*); approximately 1.2 liters of whole blood go through the nephrons each minute. This is called effective renal blood flow and is about one-third of the total cardiac output. No other tissue or organ except the lungs can claim a proportionate amount of blood. Renal blood flow is highly variable and is very easily and quickly adjusted to decreased circulating blood volume and to cardiac inadequacy, especially in chronic anemia and orthostasis. In shock, intrarenal vasoconstriction may be so prolonged that irreversible kidney damage may occur (Chapter 14). Therefore, the kidneys (and liver) play an important role in increase or decrease of blood volume, often at their own deleterious expense.

The kidney shows very little fluctuation in its oxygen arteriovenous difference in spite of the wide variations in blood flow. Thus the variation in oxygen consumption is a function of blood flow.

The rate of formation of glomerular filtrate is about 125 c.c. per minute, or about one-fifth of the effective renal plasma flow is concerned with glomerular filtrate. After the formation of glomerular filtrate, the plasma, with proteins which have been concentrated nearly 20 per cent, flows into the efferent arteriole and then into the capillaries about the tubules. Here there is reabsorption of a large portion of glomerular filtrate, formation of ammonia, and elimination of waste products by failure to reabsorb them. Most of the filtrate is attracted back through the tubular epithelium because hydrostatic pressure is reduced and osmotic pressure of plasma is increased. Ninety per cent of water and salts are reabsorbed this way. Urea, chlorides, and inorganic phosphates are the principal waste products not reabsorbed in proportionate fluid. All except 1 to

2 per cent of the remaining 10 per cent of the fluid of the glomerular filtrate is reabsorbed by the tubular epithelium because of the presence of the antidiuretic hormone of the posterior lobe of the pituitary gland. Only 1 to 2 per cent of the glomerular fluid goes into the bladder. This accounts for the 2 liters of urine a day. One per cent of 125 c.c. equals 1.2 c.c. per minute or 70 c.c. an hour or 1,800 c.c. in twenty-four hours (Talbott).

When water is drunk, the preformed antidiuretic hormone gradually disappears from the circulating blood. But for about thirty minutes it is present in sufficient quantity to restrain the kidney. After its concentration diminishes, the rate of urine formation increases. When, as a result of diuresis, water excess is removed, the secretory activity of the pituitary increases again and the formation of urine diminishes. The stimulation is thought to be through the central nervous system (see Chapter 11).

Approximately 90 per cent of the sodium and chloride in the glomerular filtrate is reabsorbed due to osmosis of the remainder that is reabsorbed hormonal control takes hold. Adrenal cortex, estrone, progesterone, and testosterone may play a role. Cortin is perhaps most important (see Chapter 22). If cortin is absent, normal amounts of salt are not reabsorbed.

Rehberg groups the glomerular filtrate into three classes: (1) substances which are actively reabsorbed (high threshold). They are substances which are conserved to the body and are usually in lower concentration in the urine and in higher concentration in the reabsorbed fluid than in the plasma (glucose, Na, K, Ca, Mg and Cl). (2) Substances which pass back through the tubular epithelium by a simple process of diffusion when their concentration in the tubular fluid rises above their concentration in the plasma (low threshold substances)—(urea, uric acid, and phosphates). They are not actively reabsorbed. Forty to 50 per cent of the filtered urea is returned to the blood in this way. (3) Nonthreshold substances which are not actively reabsorbed or diffused back into the blood. They are absent from the reabsorbed fluid.

Diuresis occurs as a result of the complex mechanisms already described, and, in addition, it may be stimulated by certain substances which are said to act as diuretics. The exact method by which they accomplish this is not known in every case, but in general their action falls into the following groups: (1) osmotic diuretics such as *dextrose, sucrose, urea* are present in high concentrations in glomerular and tubular urine, and because of their intrinsic osmotic pressure, they prevent normal reabsorption of water and salt. *Sodium sulfate* prevents reabsorption because tubular epithelium is impermeable to it; the same is true of acid forming salts (ammonium chloride, ammonium nitrate, calcium chloride) and neutral salts (sodium chloride, potassium chloride, and potassium nitrate). (2) Xanthine diuretics (caffeine, theobromine, theophylline)—*caffeine*, which increases the chloride concentration and lowers the concentration of urea in the urine (although the absolute amount of urea excreted is increased), was formerly thought to act by increasing kidney blood flow. Xanthine diuresis probably results from decreased tubular absorption of fluid and a small increase in glomerular filtration. (3) Reduced re absorption—mercurial diuretics such as Salyrgan, mercurous chloride, merbaphen, Mercurin, Mercupurin all act by preventing or reducing tubular reabsorption of water. (4) Paralysis of tubular function—*phloridzin* produces polyuria and glycosuria in this manner. (5) Miscellaneous and combination diuretics. Digitalis is not a diuretic but in cardiac failure with edema the improved circulation results in diuresis. Water is the best diuretic known and acts by decreasing osmotic pressure, increasing hydrostatic pressure, and depressing the antidiuretic hormone. However in water balance its action is influenced by electrolytes, acid-base balance, and other factors (see Chapter 11). Acidifying salts such as ammonium chloride and calcium chloride act not only by their osmotic, but also by their acid-base balance effects (Chapter 12). Glucose must be in high concentration to act as a diuretic; this explains in part the polyuria of diabetes. The diuretic action of plasma and whole blood in hypoproteinemia and hypotension states is discussed in Chapters 11, 13, and 14.

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adequate fluid intake, excessive fluid loss as in intestinal obstruction, or severe diarrhea. (5) Severe alkalosis due to its causes (vomiting), loss of base by urine, thereby depleting water stores and tetany. (6) Hypernatremia and retention of water (salt block). (7) Cardiac failure which causes hypotension, engorgement of renal vessels, and slowing of renal blood flow and stagnant anoxemia. (8) So-called hepatorenal syndrome probably due to peritonitis, dehydration, and hepatic insufficiency.

II. Renal anuria "lower nephron nephrosis," "*hemoglobinuric nephrosis*," may be due to: (1) The extreme congestion of acute nephritis. (2) Posttraumatic or "crush syndrome" with myoglobin and hemoglobin casts, necrosis of the epithelium of the distal convoluted tubules said to be due to vasoconstriction in renal cortex. (3) Bilateral cortical infarction, postoperative. (4) Incompatible (hemolytic) transfusions. (5) Transurethral prostatectomy with water used as an irrigating fluid which may cause intravascular hemolysis. (6) Sulfonamide crystals blocking tubules. (7) Degenerative nephritis (mercury, lead, phosphorus, carbon tetrachloride). (8) Severe hemolytic infections, "black water fever," severe septicemia due to hemolytic streptococcus (other factors as enumerated in I. also enter into this type). (9) Polycystic kidneys. (10) Severe pyelonephritis. (11) Bilateral renal tuberculosis (severe).

III. Postrenal anuria is due to blockage of the ureters by: (1) Stones. (2) New growth. (3) Sulfonamide crystals. (4) Sometimes oliguria or anuria may follow instrumentation probably through reflex causes. (5) Surgical severance of both ureters. (6) Large pelvic or abdominal tumors blocking the ureter. (7) Vesical carcinoma involving both ureters. (8) Congenital anomalies involving both ureters.

The pathology of the different types will vary with their cause. In group I, degeneration of the tubules is said to occur in about twenty-four hours, followed by necrosis of tubule cells. Regeneration occurs in ten to twelve days and is normal in about four weeks. The symptoms and signs will vary with the different causes. However, the type seen most commonly belongs in group I. Since this type will be encountered following surgery or injury, it will be unsuspected for the first few hours because the primary or causative state will mask the symptoms. However, this is the time during which injury occurs. Urinary output will be depressed, but here again this is the rule following prolonged anesthesia or during or following shock states from any cause. Soon it will be observed that oliguria persists or changes to anuria. Azotemia follows. The little urine that is put out has a low specific gravity (1.005 to 1.010), chlorides are low, albumin is present, and there are red cells, white cells, granular casts (with or without degenerated hemoglobin or myoglobin), and heme casts (after incompatible blood transfusions). Blood studies show high urea, nonprotein nitrogen, and *creatinine* valves, but there may be a disproportion between the urea elevation and

The Mechanism of Kidney Hypertrophy.—When one of two kidneys is removed, the surviving organ increases in size, in proportion to the increase in the functional demand made upon it. The hypertrophy of kidney tissue is due to hypertrophy of the glomeruli with hypertrophy and hyperplasia of the cells of the tubules and not to regeneration of new elements (nephrons). Factors determining the degree of hypertrophy are as follows: (1) The greater the proportion of total renal substance resected, the greater is the hypertrophy of what remains. (2) The degree of growth is greater on a high than low protein diet. (3) The retention of urinary products in the blood (achieved experimentally) has been shown to hasten and increase the hypertrophy which occurs following unilateral nephrectomy. While no particular substance has been demonstrated, it has been noted that blood urea and the phosphates and sulfates were markedly increased. (4) Testosterone propionate increases kidney weight.

Functional compensation of the remaining kidney for the loss of the other is almost immediate and precedes by several weeks the structural compensation. After the loss of an active kidney, the following physiological changes occur: (1) Tubular excretory mass, glomerular filtration rate, and effective renal blood flow are cut in half. (2) Very soon the glomerular filtration rate and the effective renal blood flow increase considerably. (a) The early increase in glomerular filtration rate is apparently the maximum expansion of this function under these conditions. (b) But the effective blood flow continues to increase for several months—Arteriolar dilatation results in lowered intraglomerular pressure. (c) There is a relative hyperemia of tubular tissue in that the latter's increase is slower at first than is the increase in renal blood flow. (d) In one case reported, two years were required for the compensatory hypertrophy to catch up with the renal flow. After the removal of a nonfunctioning kidney, the function of the remaining kidney is about three-fourths of the average for the two normal kidneys.

Decreased Kidney Function.—This is observed normally in muscular exercise as a result of diversion of blood to the active muscles in hot weather due to excessive sweating and when fluid intake is restricted.

Oliguria and Anuria.—These are due to many diverse conditions, but the principal causes may be grouped under the following headings:

I. Prerenal anuria has also been known as "renal anoxia syndrome" and may be due to: (1) Shock from any cause where the *hypotension* is sustained long enough and filtration ceases. (2) Oliguria due to traumatic, operative, or obstetrical causes. Here anoxia and hypotension play a role. (3) Hemoconcentration as seen in burns or diffuse infections like peritonitis. There is loss of plasma, reducing the osmotic pressure, so that fluid cannot be drawn into the blood stream for excretion. Other factors are stagnant anoxemia and toxemia. At least part of the "crush syndrome" is due to loss of plasma. (4) Dehydration due to in-

toxic cases is important. Alkalinization in renal injury from sulfonamides and transfusion reaction seems helpful. BAL, 2,3-dimercaptopropanol, neutralizes mercuric chloride poisoning, and, in addition, the stomach may be lavaged with sodium formaldehyde sulfoxylate.

2. *Maintenance of as near a normal state of hydration and nutrition as possible* is necessary; however, the treatment should not be carried too far. With kidney excretion absent, the body must depend upon the lungs (about 300 c.c. daily), the skin (1,500 c.c.), and the bowel (150 c.c.) to carry the load. In addition, potassium which increases due to cellular damage is not eliminated by the damaged kidneys, permitting a dangerous accumulation of this base. Since the kidneys normally put out almost as much as all other avenues (1,500 c.c.), the fluid intake should not exceed this figure in the average adult unless added amounts are lost by vomiting, diarrhea, or other causes. Glucose reduces endogenous protein breakdown and so does plasma. Protein hydrolysates should not be used since they add to the burden of the nonfunctioning kidneys and increase azotemia. One hundred grams of glucose given daily should prevent ketosis and reduce protein breakdown greatly. Thus nitrogen waste products, potassium, sulfate, and phosphate released by protein catabolism accumulate less rapidly. The metabolism of 37.5 Gm. protein daily will lead to the formation of about 6,000 mg. of nonprotein nitrogen. This will be distribued to the body fluids which amount to about 3.5 liters in a 100 pound adult or over 17 mg. per 100 c.c. rise per day. Sodium chloride should not exceed normal requirements of 5 to 6 Gm. unless it is being lost in large quantities, lest a hypernatremia and edema result. Certainly forcing fluid to "wash out" the kidneys leads only to generalized edema including the brain and lungs (see Chapter 11). In many cases within 10 to 14 days diuresis begins. Careful watch on blood chlorides, serum protein, hematocrit will help guide in the treatment.

3. In severe cases, *provision for elimination by dialyzing or other procedures* may be necessary. This is done with the hope that the tubules will return to normal after two to three weeks. Man may survive four to five weeks without renal function if not hyperhydrated.

a. *Artificial kidney.* In lower nephron nephrosis and toxic nephrosis some method of removing diffusible substances from the blood is desirable. Most artificial kidneys use cellophane as the dialyzing membrane through which blood is circulated outside the body through a medium which will remove diffusible crystalloids but which will not take away essential substances from the blood stream. The dialysates vary in their composition but most of them contain NaCl, Ca Cl_2, Mg Cl_2, Na H_2 PO_4, dextrose, K Cl, Na HCO_3. Some remarkable cures have been reported. Indeed the method has been referred to as "parabrosis" by some.

b. *Peritoneal* dialysis seeks to convert the peritoneum into a dialyzing membrane so that diffusible substances may be removed from the plasma and ultimately from the extracellular fluid. This method is useful in severe cases of anuria, but careful planning and meticulous attention to

the creatinine. There is hyponatremia and hypochloremia, hyperpotassemia (hyperkaliumemia or hyperkalemia), usually hypoproteinemia with reversal of albumin-globulin ratio, and also anemia with low hematocrit (except in burns). In hemolytic transfusion cases, hemoglobinemia and hemoglobinuria is present for at least forty-eight hours or longer. Methemalbumin in the serum as demonstrated by spectrophotometric analysis means intravascular hemolysis. There will be slight increase in the serum bilirubin in the transfusion incompatibility as well as in the hepatorenal syndrome, the latter due to liver damage. The CO_2 combining power is decreased. The nitrogen retention and acidosis are probably not the lethal factors, but potassium intoxication may be.

During this stage the clinical picture, in our experience, is at first one of cerebral stimulation with continual loud talking which is fairly coherent and euphonic; restlessness and muscular twitchings are present. Intervals of complete rationality are present. These may progress to stupor or coma, and then there may be a return to the stage of stimulation. There is generalized and early pulmonary edema.

As diuresis returns, there is usually a diarrhea, or this may precede the diuresis. The urine contains large quantities of salt. Soon there will be a large amount of urine with increase in specific gravity. The azotemia persists for about six days and does not return to normal for two to three weeks after diuresis begins. Indeed, diuresis is not invariably followed by recovery, but it is usually, specially if the concentrating power of the kidney is restored. Slowly the patient's mental state returns to normal, although he will have no recollection of his illness.

Treatment may be considered under three headings: (1) elimination of the cause or causes to minimize damage; (2) maintenance of water, electrolyte, blood volume, and protein balance in as nearly a normal state as possible; (3) provision for elimination by dialyzing or other procedures. Put in another way, the destroyed kidney cells cannot be revitalized but damaged cells may recover. Treatment then consists of measures designed to stop the injury to tubule cells so that the extent and degree of damage will not be irreversible. Moreover, measures must not be instituted which will burden the kidney and thereby indirectly produce kidney damage. Having stopped or at least discouraged the cause of the trouble, time must be allowed for tubular cells to recover, and during this time life must be maintained by attention to water, oxygen, food vitamins, and electrolytes, and elimination of waste products must be provided for.

1. *Elimination of the causative factors* is not always easy. A list of the causes will in most cases suggest the remedies: whole blood for shock due to oliguria, water and electrolytes in dehydration, plasma in hypoproteinemia, the Miller-Abbott tube in postoperative adynamic ileus, etc. The immediate exclusion or neutralization of the causative agent in nephro-

syndromes are due to a neurogenic effect, this may be helpful. Many cases of anuria have been successfully treated by spinal block or continuous caudal block but not those due to kidney changes associated with chronic hypertension.

The Kidney Pressor System.—*Hypertension* has many causes. Some are not definitely known. In Chapter 18 the role of the sympathetic nervous system in essential hypertension has been discussed. Its relationship to kidney disease is better understood. Since the two are often related, it is sometimes difficult to determine which is cause and effect. The benefits of sympathectomy in cases of hypertension are probably not due to improvement in renal circulation but rather to venous stasis, with decrease in venous return and thus a decrease in cardiac output. The relation of the renal vasopressor system to hypertension is thought to be humoral (renin) rather than neurogenic. Normal kidneys and other tissues are thought to have a substance capable of destroying or inactivating renin (angiotonin). Prior to the surgical treatment of coarctation of the aorta, the hypertension, although largely confined to the upper extremities, was thought to be due to the decreased blood flow to the kidneys. This is now known to be erroneous in many cases. However, in some despite the release of the obstruction and improved blood flow to the lower extremities, the hypertension is not relieved and continues to progress. The role of the liver in hypertension is discussed in Chapter 22.

There is, however, much experimental evidence that interference with the circulation of one or both kidneys may result in the liberation of a pressor substance into the blood stream with resulting hypertension. This substance has not been demonstrated in the peripheral circulation of human beings or experimental animals with hypertension. Nevertheless, hypertension associated with unilateral kidney disease in man is sometimes cured by nephrectomy. The commonest pathological condition is pyelonephritis, but no specific lesion is more apt to be causative than another, and no prediction can be made on the effect of nephrectomy on the hypertension. However, compensatory hypertrophy of the healthy kidney is a good indication of a favorable result. The younger the patient and the shorter the duration of the hypertension, the better the results.

Organic Diseases and Injuries of the Kidneys, Ureters, and Bladder

Congenital Malformations of the Kidneys.—These are usually multiple and may occur due to failure of the proper fusion between the tubular structures and the renal parenchyma at the level of the collecting tubules, giving rise to *polycystic kidneys*, or *solitary cysts* may form, the former resulting from faulty fusion between the collecting and convoluted tubules or from persistent primary tubules of the metanephros. Most cysts are therefore glomerular or secreting tubular. Some are excretory tubular due to fibrous occlusion of the collecting tubules. There may be *supernumerary arteries* or vessels, due to the persistence of some of the

details are necessary. Some of its hazards are electrolyte unbalance, excessive loss of glucose, peritonitis, fibrin deposition around the afferent and efferent tubes, leaving only a small channel along the path of the dialyzing fluid instead of the whole peritoneal cavity, edema, and acidosis. To combat the ill effects of this method, the irrigating fluid is composed of a modified Tyrode's solution (Na Cl 7.4 Gm. per liter; K Cl, 0.2; Ca Cl_2, 0.2; Na HCO_3, 1.0; gelatin, 10.0; Mg Cl_2 . 6 H_2O, 0.22). Glucose is added to prevent the loss of blood sugar, heparin is used to delimit fibrin deposition, and penicillin and streptomycin are used to prevent peritonitis. Edema frequently occurs in this method, because there is absorption of some of the irrigating fluid (anywhere from 2 to 8 per cent and excess of sodium. However, the acidosis of uremia is not usually corrected unless it is treated by intravenous solutions of glucose (to impede ketosis and reduce protein catabolism) and alkali. Large volumes of fluid must be used (30 to 60 c.c. per minute), and this may be continuous or intermittent (the latter is probably preferable). To reduce the nonprotein nitrogen by one-half in forty-eight hours, the blood urea clearance (by peritoneal clearance) through peritoneal irrigation must be at least 20 c.c. per minute.

c. *Intestinal lavage* is one of the oldest methods employed to rid the body of nitrogenous and other waste products. As first employed, it consisted of diaphoresis and purgation; later, by colonic irrigation; and more recently, the stomach, duodenum, jejunum, and ileum have been used for dialyzing purposes. The methods employed are the use of double lumen tubes passed through the nose or mouth or the creation of enterostomies or cecostomy. These methods are safe and easy to use but are not very effective.

d. *Renal decapsulation* is used with the idea of decreasing intrarenal pressure which presumably interferes with effective filtration in toxic nephrosis because the net or effective filtration pressure is reduced. Although this procedure reduces intrarenal pressure, this fact alone is probably not the sole cause of improvement in the case reported, because spontaneous diuresis usually occurs in favorable cases on the tenth to twelfth day, when fluid retention is at a maximum. Interruption of the sympathetic nerve supply to the kidney by this procedure is thought to be the reason for its apparent effectiveness in some cases. Decapsulation of one kidney gives as good results as bilateral decapsulation.

e. *Plasmapheresis and reciprocal transfusions* have been used in Rh and other blood transfusion incompatabilities and also in toxemias of pregnancy with anuria. The method is hazardous because of the depletion of blood proteins temporarily and also because of the large quantity of blood required and its potential unfavorable reaction.

f. *Spinal anesthesia or splanchnic block.* Reflex stimulation of the splanchnic nerves can divert blood from the cortical glomeruli. After section of these nerves, the effect is reversed. If crush and other allied

jection of substances into the ureter under pressure may give rise to pyelovenous backflow. This has been observed in making pyelograms. The phenomenon has been explained by assuming an actual connection between the kidney pelvis and the veins due to a tear in the latter, or by extravasation into the kidney substance and reabsorption by the veins. Should such a kidney become infected, *pyonephrosis* ensues. There may be supernumerary kidneys, usually one but sometimes two on each side. Agenesis (complete absence), aplasia (defective formation), hypoplasia, and hypertrophy also occur. The kidney may fail to ascend (pelvic kidney, ectopia, or dystopia), or may rotate, allowing the pelvis of the kidney to face anteriorly or posteriorly instead of medially. Sometimes

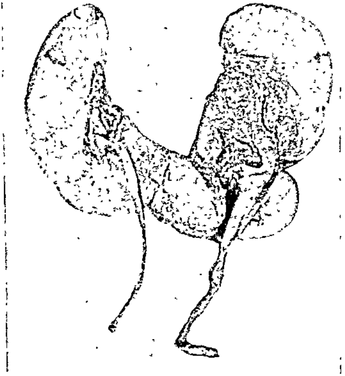

Fig. 414.—Horseshoe kidney. This illustrates the result of fusion of the fetal kidneys at the lower poles. Such anomalies prevent ascension and rotation, so that the pelves face anteriorly and the kidneys lie low in the bony pelvis The notch at lower right is due to an anomalous vessel.

the lower poles of the two kidneys fuse across the midline, forming a *horseshoe kidney,* or both kidneys may be on the same side without fusion (crossed ectopia). Other changes in form include sigmoid kidney, disc kidney, lump kidney, and anteroposterior fusion. If the kidney is unusually *movable,* it may produce a kink in the ureter, giving rise to *dietl's crisis,* or *intermittent hydronephrosis.* Diagnosis of these lesions is by physical examination and by intravenous and retrograde pyelogram through the cystoscope. Surgery aids these conditions. Polycystic kidneys are not very amenable to treatment (although solitary cysts may be

many vessels from the primitive aorta which supply the kidney in its development and which normally disappear, leaving only the renal artery and vein. Supernumerary arteries impede the passage of urine down the ureter, giving rise to hydronephrosis or to a dilatation of the renal pelvis and calyces. Normally urine is propelled into the bladder by the peristaltic movement of the ureter. Mild impediments may be overcome by ureteral hypertrophy and strong "peristaltic" waves. Intravenous pyelograms are helpful in making the diagnosis. If the dye outlines the ureter, there is interference with ureteral propulsion. Normally the ureter is not demonstrated.

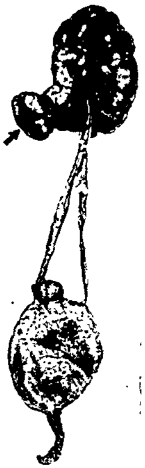

Fig. 413.—A type of congenital anomaly. The right kidney is rudimentary, misplaced, and fused with the lower pole of the left kidney. Arrow points to rudimentary mass. Note fetal lobulations. Post-mortem specimen.

According to Cohnheim's law, a complete obstruction of the duct of an organ gives rise to atrophy. The organ becomes distended and the increased pressure causes interference with the venous return. The mechanism is the same as in Volkmann's contracture of the hand and arm. Arterial blood enters, while intravenous pressure mounts, giving rise to stasis, local asphyxia, and death of the tissue, with fibrosis. In-

Injuries.—Injuries may occur to the urethra, bladder, or kidneys. The diagnosis is made from a history of trauma, with identification of the site of the injury, from blood in the urine, or from discovery of a palpable mass in the kidney. The x-rays reveals dense shadows where blood has extravasated. Treatment may be conservative in minor injuries. For lacerations in the kidney or bladder, surgical repair is necessary. Often nephrectomy must be done. In all bladder injuries adequate suprapubic drainage is helpful.

Infections of the Kidney and Bladder.—Like infections elsewhere, infections of the kidney and bladder do not usually occur when there is free drainage. This is as true of a sebaceous gland as of the kidney, and as true of the gall bladder as of the urinary bladder. The local immunity of the urinary tract is extremely high, unless there is devitalization of cells due to trauma or obstruction which, as we have seen leads to devitalization. Stasis alone would probably cause a collection of fluid, but when it reaches a point where it interferes with blood supply, and hence with cell metabolism, infection ensues.

To prevent stasis, the urinary tract, through involuntary muscle in the renal pelvis and the ureter, exhibits a wave of contraction resembling peristalsis. The bladder empties itself often enough to prevent stasis also. The cause of stasis may be (1) pressure from without by bands, aberrant vessels, new growths, collections of pus, etc.; (2) disease in the walls of the channels, such as strictures, inflammations, kinks, new growths; (3) improper nerve control, which causes interference with function; (4) partial or complete obstruction within the lumen of the channel by congenital folds, neoplasms, or calculi; (5) ureteropelvic obstructions due to external causes (kinking, distortion by adhesions, fibrous or vascular bands, and anomalous vessels) and internal causes (stricture at ureteropelvic junction, valve formation due to high insertion of ureter); (6) vesical neck obstructions in men (usually prostatic hypertrophy) and in women (due to fibrosis) and associated with chronic cystitis; (7) stenosis following ureterosigmoidostomy or external ureterostomy. The diagnosis is established by a careful history, the symptoms and signs, x-ray studies, intravenous, and retrograde pyelography. Treatment consists of (a) an attempt to remove the cause if possible, (b) if not, adequate drainage may be secured by (i) plastic repair (pyeloplasty, ureteroplasty), (ii) short circuiting (ureteropyeloplasty, ureteroenterostomy), (iii) external drainage (pyelostomy, ureterostomy, cystostomy); (iv) removal of the kidney as a last resort.

Infections rarely, if ever, start in the kidney or bladder but are usually carried to the kidney by the blood stream, from neighboring tissues (for example, the bowel), and by the lymphatics unless there is obstruction to urinary excretion. So-called nonspecific infections are due to mixed organisms—*Staphylococcus aureus*, streptococci, and colon bacilli.

removed). Therefore, patients with polycystic kidneys die from either renal failure or hypertension. Retention cysts may be relieved by the division of aberrant vessels or by moving the kidney and anchoring it in such a way as to prevent obstruction. Sometimes the renal pelvis is anastomosed to the ureter around an obstruction. Horseshoe kidneys may be divided if sufficient pedicle exists, or if one kidney is much larger than the other.

The *ureters* may be double, or they may be narrowed near the ureteropelvic juncture. Treatment in the former case may be unnecessary, or one ureter may be removed. Ureteral dilatation may be required for the latter. Sometimes they end in the urethra or vagina and are associated with supernumerary kidneys. Thus the ureters may be abnormal as to their number, position, or place of implantation. Other anomalies include congenital atresia and stenosis, congenital valves, diverticula, kinks of the ureter and ureterocele (a cystic dilatation of the intravesical part of the ureter). Any of these anomalies may lead to obstruction, dilatation, infection, and calculus formation in the ureter and ultimately hydronephrosis and pyonephrosis.

The treatment for these anomalies is primarily directed to relieve the obstruction so that the kidney may be preserved. This is accomplished by dilatations, short-circuitings, resections of abnormal parts, reimplantation, and various changes in position to relieve kinks and pressure from anomalous vessels. The *bladder* may have diverticula which require surgical excision. The urachus (the part of the allantois extending from the umbilicus to the cloaca, the anterior part of which later becomes the bladder) may persist *in part*, causing cystic formations, or *in toto* as a fistula from the bladder through the umbilicus. Such lesions may be excised extraperitoneally as a rule (see Chapter 20). Rarely, the anterior *abdominal wall between the umbilicus and the symphysis* pubis fails to unite, giving rise to *exstrophy of the bladder*. When this happens in the male, the external genitals are usually split anteriorly—*epispadias*. Since the anterior bladder wall is absent, urine dribbles over the area, causing excoriation and infection. Treatment is by transplantation of the ureters into the sigmoid, followed by excision of the bladder wall and repair of the abdominal wall. We have usually transplanted both ureters at the same time, using Sulfasuxidine to prepare the bowel before surgery. Small Penrose drains are introduced through the loin and extended *retroperitoneally* to the site of transplantation. The operation is due as soon as there is bowel control (18 months to 2 years). The second stage is deferred until the age of 4 or 5 years. After mobilizing the bladder mucosa and repairing the abdominal wall defect, a portion of the mucosa is saved to form an anterior wall for the urethra. The superior surface of the penis is covered with skin which is brought backward from a flap of the foreskin. Thus the full length of the urethra is maintained so that the reproductive tract may be established.

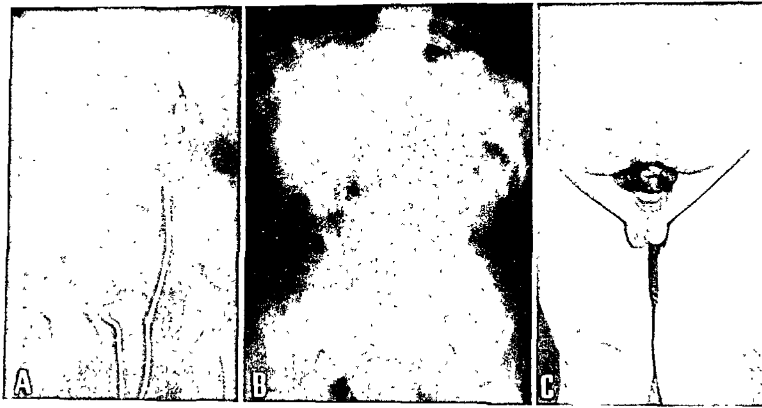

Fig. 416.—Exstrophy of the bladder and epispadias. *A*, Preoperative retrograde pyelogram. *B*, Six months after operation an intravenous pyelogram was made. It will be noted that the right ureter is normal. The left ureter shows a slight amount of dilation although not enough to be of consequence. *C*, Clinical photograph of child with extrophy of the bladder following the first stage operation which consisted of bilateral transplantations of the ureters into the sigmoid colon. The operation was done through a lower midline incision, although a transverse incision may be employed. The ureters were divided and transplanted into the colon on both sides. The lateral flaps of peritoneum were dissected to the pelvic wall, and extraperitoneal stab wound drainage was established in both loins. The free margins of the peritoneum were then closed over the inserted ureters.

No attempt was made to tunnel the ureter. Instead it was split and anastomosis was attempted between the mucosa of the ureter and the bowel, then there was an infold of serosa over the transplanted ureter, and, lastly, the free fold of peritoneum was sewed down over the transplant. The child is in perfect health, and a second stage operation will be done, excising the remaining bladder mucosa and correcting the epispadias. (*Referred by Dr. Francis T. Brown.*)

In this group are the following: (1) Carbuncle of the kidney, which is a collection of pyogenic abscesses in the kidney parenchyma secondary to primary foci elsewhere and carried by the blood stream (pyemia). Such foci include boils, osteomyelitis, and otitis media. (2) Perinephritis and perinephric abscess which are infections of the perirenal fatty tissue. The infection occurs *secondary* to hematogenous foci from various parts of the body or by extension from the kidney or other adjacent structures (vertebrae, lungs, pleura, appendix, colon, and pelvic organs). (3) *Pyelonephritis* which is an infection of the kidney pelvis and parenchyma. Pyelitis was a term used to denote infection of the kidney pelvis alone, a condition which probably does not occur. The disease may be acute, chronic, or recurrent. It is due to hematogenous or ascending infection from the lower urinary tract due to urinary obstruction. Sometimes

Fig. 415.—Exstrophy of the bladder, with epispadias, in an infant. There is also a prolapse of the rectum.

both factors are present. In children (usually girls) congenital anomalies may be causative; in pregnancy the disease is commonly thought to be due to ureteral spasm, or pressure and hematogenous causes. In adult males calculi are the most common cause. (4) Pyonephrosis—a term used to describe the hydronephrotic kidney with infection. (5) Kidney infarction due to endocarditis which may result in secondary infection with abscess formation. (6) Trauma with kidney tears which may be followed by infection.

Symptoms and signs: A careful history often leads to the diagnosis. Attacks since childhood, kidney colic, and associated disease in adjacent organs are some of the common stories. In addition, there are the following: (1) pain in the kidney region which radiates along the course of the ureter; (2) urgency and frequency if an associated cystitis is

Fig. 418.—Pyonephrosis of the kidney. Patient was a woman aged 46 years. Arrow points to the dilated pelvis, which was filled with pus.

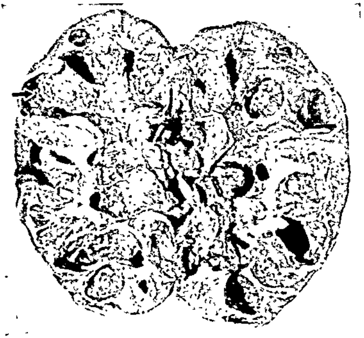

Fig. 419.—Pyonephrosis of the kidney Arrow points to the dilated calyx. Note the extreme degree of destruction of the parenchyma and the thin cortex.

present; (3) general symptoms of infection, chills, fever, malaise, and anorexia; (4) laboratory studies (urinalysis, blood cultures, and blood counts); (5) plain x-ray of kidney, ureter, and bladder; (6) intravenous urography; (7) retrograde pyelography.

Treatment: If the cause can be eliminated, there is a good chance of cure. Kidneys seem to have a remarkable regenerative ability. The elimination of an acute focus or adjacent abscess plus the establishment of good drainage where this is impaired are the major forms of attack.

Fig. 417.—Traumatic rupture of the kidney. The patient, a man aged 60 years, was in an automobile accident. Nephrectomy was done. Arrow points to the tear.

In addition, penicillin, streptomycin, aureomycin, and the *sulfonamides* are necessary. Local abscess may demand drainage, and persistent obstructions may necessitate temporary surgical drainage (pyelostomy).

If the kidney is hopelessly destroyed, nephrectomy may be indicated. *Bilateral cortical necrosis* is a rare lesion seen in pregnant women but also in nonpregnant women and in men. It is associated with septicemias and with infections which arise in the debilitated and also in children. The more common accompanying diseases are scarlet fever, diphtheria, pneumonia, tonsillitis, tuberculosis, and severe dysentery.

may arrest the disease. Before any surgery is done, the disease should be treated by medical means. This includes the general treatment of tuberculosis and the use of streptomycin. *Remissions and even cures* are not uncommon under this management.

Cystitis.—Cystitis is not an uncommon postoperative complication. The inability of patients to void, whether for psychic, reflex, or mechanical reasons, constitutes an obstruction, even though it may be only the function of the sphincteric mechanism which is at fault. Some maintain that this type of cystitis is due to overdistention and advise early and frequent catheterization. Others believe it is the trauma inflicted by the (sterile) catheter that starts it. Or perhaps it is the sudden removal of large amounts of urine from an overdistended bladder. This subject has been discussed previously in this chapter and is mentioned here as a cause of cystitis. *Acute cystitis* is due to other causes such as (1) ascending by instrumentation or catheterization, (2) descending from the kidneys, (3) contiguity from adjacent organs, (4) external trauma (fractured pelvis with perforation, penetrating, or perforating wounds).

Gangrenous cystitis may result from pressure by a pregnant uterus. A generalized form is seen in men with prolonged internal or external bladder pressure and vascular occlusion. *Proliferative cystitis* is a form of chronic infection with excessive granulation tissue. There are several varieties: (a) cystitis follicularis (lymphoid follicles), (b) cystitis granulosa and polyposa (protrusion of granulations), (c) cystitis glandularis (glandlike protrusions), (d) cystitis cystica (cystlike gland spores), (e) cystitis emphysematosa (gas-producing bacteria produce spaces in the tunica propria). *Chronic interstitial cystitis* (Hunner's ulcer) occurs in the submucous and intermuscular connective tissue of the bladder. The cause is not definitely known, but the disease is chronic and difficult to cure. *Incrusted cystitis* is due to the deposit of magnesium and ammonium phosphates derived from the bacterial action on urea. *Tuberculosis cystitis* is almost always secondary to renal tuberculosis. *Malakoplakia* is a chronic cystitis occurring in middle-aged women. It resembles Boeck's sarcoid. *Blastomycosis, actinomycosis,* and *monilia* infections are rare. *Schistosomiasis* is seen commonly in some tropical countries. *Chemical cystitis* is known to occur from *aniline* dyes. The symptoms and signs of cystitis are urgency, frequency, dysuria, pyuria, nocturia and the general reaction to infection. Diagnosis is established by a careful history, general physical examination, study of the urine and blood, and cystoscopy. Treatment is designed to eliminate the cause where possible. In addition, chemotherapy and antibiotics are used. Local treatment consists of adequate drainage where necessary, fulguration, or local cauterization of chronic lesions.

Calculus.—Urinary calculi may develop around foreign bodies, mucous plugs, or cellular debris, or de novo. Calcium phosphate is present in some stones and is said to be associated with hyperparathyroidism. Ex-

Granulomatous Diseases of the Kidney.—*Syphilis* is rare and exists as a diffuse parenchymatous or interstitial infection or gumma. Actinomycosis is also rare and is secondary to lesions of adjacent structures.

Tuberculosis of the Kidney.—This is considered in Chapter 8. It is probably a blood-borne infection, secondary to tuberculosis elsewhere. Some maintain that tuberculosis often originates in the epididymis or seminal vesicles and ascends by retrograde lymphatic involvement to the

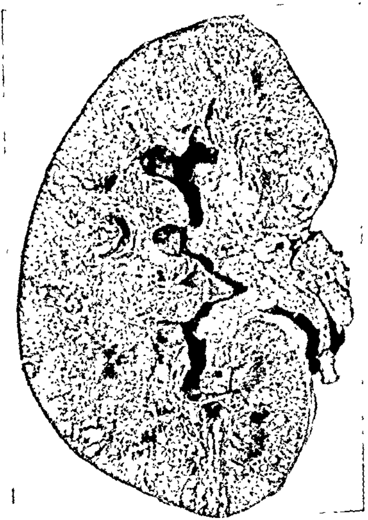

Fig. 420.—Miliary abscesses (pyemia) of the kidney. These developed in the course of a staphylococcic bacteriemia.

kidney. The early symptoms are those of cystitis: urgency, frequency, stranguria, and hematuria. The diagnosis depends upon a careful history, physical examination (which usually reveals evidences of the disease elsewhere), laboratory tests (such as the von Pirquet and Mantoux), a finding of tubercle bacilli in the urine, and, most important, cystoscopic examination and pyelography. Guinea pig inoculation with the urine may aid in the early diagnosis. The kidneys, the ureters, and the bladder are frequently involved, usually only kidney first; therefore, nephrectomy

and usually pus. Many of these attacks may occur until the stone returns to the kidney pelvis, or descends into the bladder, or is passed through the urethra.

Diagnosis is conclusively made by x-ray and pyelography. Renal colic on the right side may simulate appendicitis. If the inflamed appendix is retrocecal, it may cause pyuria by causing a ureteritis. X-ray films of the abdomen, the site of pain and tenderness, and the history aid in differential diagnosis. The treatment during colic consists of bed rest and relief of pain by the use of sodium nitrite, morphine, or calcium chloride intravenously. Passage of the stone may be facilitated by ureteral catheterization and the injection of glycerine. Should this fail, surgery is indicated. According to the location of the stone, an incision is made in the kidney (nephrotomy), in the pelvis of the kidney (pyelotomy), or in the ureter (ureterotomy), and the calculus is removed. It is unnecessary to close these openings in the kidney, pelvis, or ureter, but drainage must be used.

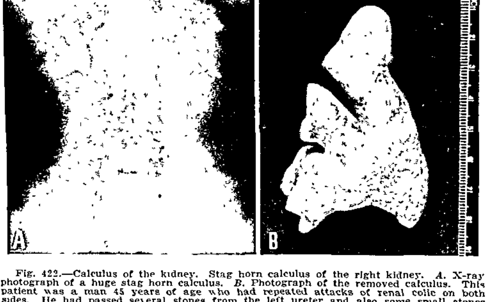

Fig. 422.—Calculus of the kidney. Stag horn calculus of the right kidney. *A.* X-ray photograph of a huge stag horn calculus. *B.* Photograph of the removed calculus. This patient was a man 45 years of age who had repeated attacks of renal colic on both sides. He had passed several stones from the left ureter and also some small stones from the right The large calculus on the right was removed through a loin incision. A nephrectomy was necessary because of the destruction of the kidney parenchyma.

Surgery of the kidney requires adequate exposure. Since most of these cases are infected, a retroperitoneal approach is desirable. Resection of the eleventh and twelfth ribs and a subcapsular approach facilitate maneuvers and reduce the possibility of pleural or peritoneal injury. Renal tissue must be handled gently; and any tear must be carefully avoided by an incision if the stone is wedged or is staghorn in shape. A pedicle clamp controls bleeding during this maneuver. Tears and incisions must be carefully closed so that postoperative bleeding will not

perimentally, stones may be produced in animals by excessive amounts of vitamin D. However, most stones are composed of uric acid, urates, oxalates. Some are made of cystine, xanthine, and magnesium ammonium phosphate, concentrated urine; urinary stasis (immobilization in bed as in burns and fractures, obstructions to urinary outflow), infection, and diet (alkaline ash, avitaminosis of A and B, high calcium) may also play a role in the formation of calculi.

"Renal rickets" is a disturbance of calcium metabolism in which *there is rarefaction of bones. The serum calcium is low and the serum* phosphate high due to the fact that the kidney cannot excrete the latter. A rise in the serum phosphate causes a reciprocal reduction in the calcium, which is excreted to some extent in the urine. As a result of this calcuria, stones may occur (see Chapter 22).

Fig. 421 —Opaque kidney stones revealed by flat plate of the abdomen without aid of dye or pyelogram.

Urinary calculi vary in size from minute granules to stones so large that they fill the bladder. They may cause obstruction anywhere *along* the urinary tract except the bladder, or they may remain in the kidney pelvis or bladder, associated with infection. Calculous anuria, hydronephrosis, ulcerations, or pyonephrosis may develop.

Clinically, a stone may be "silent"; that is, it may cause no symptoms unless it moves into the ureter. Here it causes extreme pain (renal colic) by distending this tube. This pain radiates rather typically along the course of the ureter into the genitals. *The urine is filled* with blood

more plausible. Pain in the flank may be due to inflammatory lesions as previously described, and when bilateral is more easily distinguished as due to inflammation than when present on one side. A mass in the flank may be due to an enlarged spleen (especially in children), neoplasm of the colon, sympathicoblastoma of the adrenal, chronic cystic fibrosis of the kidney, hydronephrosis (congenital in children or acquired in adults), polycystic kidneys, retroperitoneal sarcoma (in children).

Hematuria may come from many sources. It may originate anywhere along the genitourinary tract or may come from systemic causes. In general, the causes fall into the following groups, whether the seat of the trouble is in the kidneys, ureters, bladder, or urethra: (1) congenital malformations such as polycystic kidneys, (2) systemic causes, (3) infections, (4) new growths, (5) foreign bodies (calculi), (6) obstructions due to movable kidney, aberrant vessels, etc., (7) varicosities. Treatment consists of early surgical removal of the involved kidney.

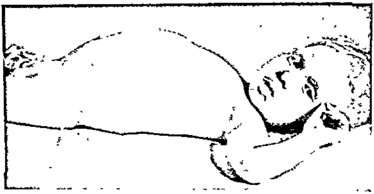

Fig. 423.—Wilms' tumor of the left kidney in a child. Treatment by x-ray reduced its size There was recurrence within nine months, resulting in death.

This should be done through the abdomen so that the renal vessels may be ligated and divided before there has been any manipulation of the growth. In this way tumor cells in the involved vein will not be separated and allowed to migrate to the lungs. In smaller growths this preliminary step may be accomplished through a loin incision. The same maneuver may be done through a long McBurney incision with resection of the twelfth rib and mobilization of the peritoneum medially as is done in lumbar sympathectomy. The important fact to remember is that with an adequate exposure (best through the abdominal cavity), tumor masses in the renal vein or vena cava may be recognized and resected, manipulation before ligation is minimal, and retroperitoneal lymph nodes may be removed. The ureter is not usually involved in parenchymal neoplasms. In tumors of the renal pelvis, however, nephrectomy with removal of all of the ureter and the adjoining corner of the bladder is indicated. This may be done through the abdomen, the loin, or by a combined approach.

occur. Resection of damaged renal tissue is preferable to suture of this substance which will slough. *If an obstruction of the ureteropelvic juncture remains, it is treated by plastic repair.* X-ray at the time of operation will disclose overlooked particles of calculi. The wounds are drained and in the case of nephrostomy or pyelostomy tubes, solutions "M" and "G" may be used for irrigation.

New Growths of the Kidney

New growths of the kidney may be benign or malignant. Benign tumors may arise from epithelial elements (adenoma, papilloma) *blood vessels* (*hemangioma*), *fat* (*lipoma*), connective tissue, muscle (*leiomyoma*), nerve tissue (neurofibroma). Malignant neoplasms may arise from any of the above kidney components; namely, carcinoma, hypernephroma (adrenal rest), *embryoma* (*primitive embryonic tissue*—Wilms' tumor), *hemangiosarcoma*, *liposarcoma*, *fibrosarcoma*, *leiomyosarcoma*, abdomyosarcoma, myoblastoma, lymphoblastoma (reticulum cells, leucemia), neurofibrosarcoma, sympathoblastoma, and secondary malignant growths from distant foci.

Cancers may be further classified as to their position as follows:

1. *Renal parenchymal tumors: (a) clear-cell carcinoma; (b) granular-cell carcinoma*—sometimes (a) and (b) occur together and show *various* architectural arrangements of renal cells (alveolar, adenomatous, tubular, papillary, or cystic formations); (c) true hypernephroma (adrenal rests); (d) neoplasms in solitary cysts; (e) multiple papillary adenoma or carcinoma in sclerotic tubular cysts or sclerotic kidneys; (f) mixed forms of carcinosarcoma in infants (Wilms) and adults.

2. Tumors of renal pelvis: (a) papillary carcinoma; (b) squamous-cell carcinoma; (c) undifferentiated carcinoma.

3. *Renal capsule malignancies:* (a) fibrosarcoma; (b) liposarcoma. *The neoplasms more commonly encountered are* hemangiomas, carcinomas, *and embryomas.*

Symptoms and signs in the order of frequency are *hematuria*, lumbar pain, and discovery of a mass. There are also anorexia, *loss of weight*, chills and fever, leucocytosis, and secondary anemia. The *diagnosis is* established by a study of the urine, especially by means of smears of fixed urinary sediment; that is, the urine is centrifuged and the sediment is fixed and stained (see Chapter 2). In this way desquamated cells may reveal early "carcinoma in situ." Intravenous pyelograms will reveal function, and *retrograde pyelograms will disclose* pathognomonic morphology. X-ray studies of the lungs and long bones may show metastases because malignant neoplasms of the kidneys spread by the lymphatics and the blood stream as well as by contiguity. Since the three cardinal *symptoms* are pain in the flank, hematuria, and a mass, each is subjected to careful *investigation*. A combination of the three makes the diagnosis

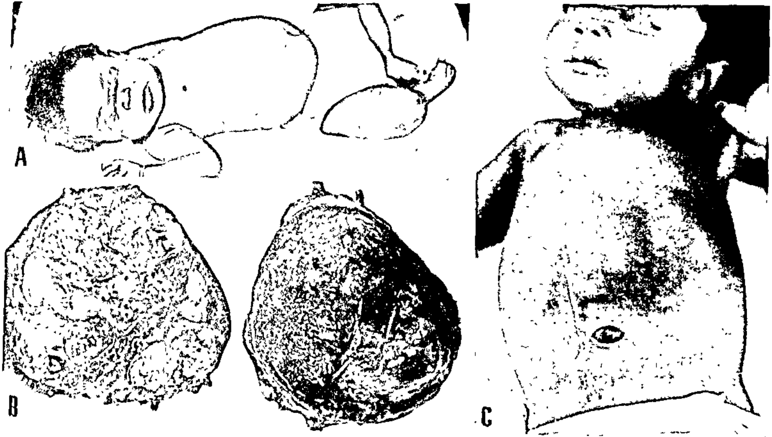

Fig. 425.—Wilms' tumor. Child 9 months of age with a Wilms' tumor of the right kidney. The mother stated that she had noticed an increase in the child's abdomen for six weeks prior to his admission to the hospital. There was no passage of blood in the urine. Studies indicated that the lesion was outside of the intestine, and retrograde pyelograms showed the lesion to be in the kidney. *A*, Clinical photograph made before operation showing enormous swelling of abdomen. *B*, Gross specimen cut in half. *C*, Postoperative condition two weeks following surgery. This child is now 2 years of age and is without detectable recurrence. There was no preoperative x-ray therapy. However, extensive postoperative x-ray therapy was given.

The operation was performed through a transabdominal approach where the renal vein was freed and the renal artery clamped and then the renal vein divided close to the vena cava. Division of the vein was done first before any mobilization of the kidney in order to avoid expressing tumor cells from the kidney. The division of the renal vein was so close to the vena cava that the latter was sutured because the pedicle was not long enough to afford a tie. Preoperative x-ray therapy has been advocated by some. However, much

The most common neoplasms which occur in the kidney *parenchyma* in childhood are the embryomas of Wilms or embryonal carcinosarcoma. They are of primitive nephrogenic tissue origin and metastasize by the lymphatics and blood stream. They may attain an enormous size and *may be bilateral. Diagnosis is made from hematuria, from finding* a mass in the kidney region, and from pyelography. The treatment is nephrectomy. Formerly, preliminary x-ray therapy was given to reduce the size. This is probably a waste of time. Transabdominal section with preliminary ligation of the renal pedicle gives the best results. We have in addition given postoperative x-ray therapy.

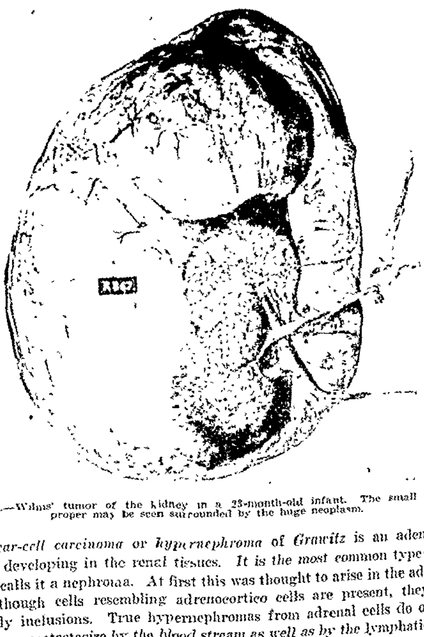

Fig. 421.—Wilms' tumor of the kidney in a 23-month-old infant. The small kidney proper may be seen surrounded by the huge neoplasm.

Clear-cell carcinoma or *hypernephroma* of *Grawitz* is an adenocarcinoma developing in the renal tissues. *It is the most common* type seen. Young calls it a nephroma. At first this was thought to arise in the adrenal but, although cells resembling adrenocortico cells are present, they are probably inclusions. True hypernephromas from adrenal cells do occur. Nephromas metastasize *by the blood stream as well as by the* lymphatics, so

TABLE XXX

TISSUE	BENIGN	MALIGNANT
Epithelial	Papilloma	Carcinoma
	Leucoplakia	
Fibrous tissue	Fibroma	Fibrosarcoma
	Myxoma	Myxosarcoma
Nervous	Neurofibroma	Neurosarcoma
Blood vessels	Hemangioma	Angiosarcoma
Fat	Lipoma	Liposarcoma
Muscle	Leiomyoma	Leiomyosarcoma
	Rhabdomyoma	Rhabdomyosarcoma
Lymphoid		Lymphosarcoma, Hodgkin's disease, reticulum-cell sarcoma, plasmacytoma
Mixed	Dermoid	Malignant mixed tumor
		Embryoma

Fig. 437.—Primary carcinoma of the kidney. Note the extension of the growth into the renal pelvis.

From adjacent organs the more common extensions are from carcinoma of the rectum and cervix and endometriosis from the tubes, ovaries, or uterus. The most common of all primary tumors of the bladder are the epithelial types, *papilloma and carcinoma*. *Although the cause of*

that very often the earliest evidence is a metastatic lesion in the lungs or the bones. Local extension also occurs into surrounding tissue but earlier in the veins as thrombotic masses. *The chief symptoms are hematuria and the palpation of a mass.* Diagnosis is by cystoscopic examination and pyelography. The treatment is nephrectomy. This may be done by the intra- or extraperitoneal approach. Even extremely large growths may be removed through the loin by a combined extrapleural, extraperitoneal approach. This is accomplished by resecting the eleventh and twelfth ribs, and, if necessary, a portion of the tenth rib. The pleura is gently pushed forward and then the lateral lumbocostal arch (external arcuate ligament of the diaphragm) is divided.

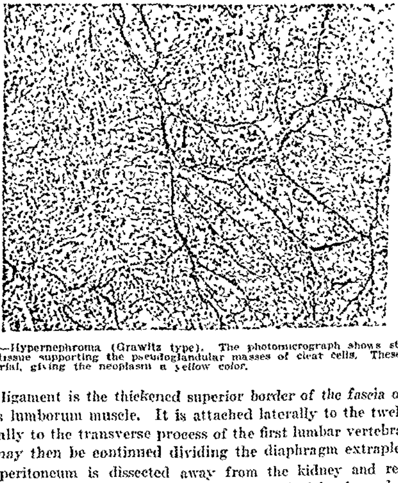

Fig. 426.—Hypernephroma (Grawitz type). The photomicrograph shows strands of connective tissue supporting the pseudoglandular masses of clear cells. These contain lipoid material, giving the neoplasm a yellow color.

This ligament is the thickened superior border of the fascia over the quadratus lumborum muscle. It is attached laterally to the twelfth rib and medially to the transverse process of the first lumbar vertebra. The incision may then be continued dividing the diaphragm extrapleurally.

The peritoneum is dissected away from the kidney and retracted anteriorly. Thus a combined thoraco-abdominal incision is made which is extrapleural and extraperitoneal and which affords ample exposure.

Tumors of the renal pelvis such as papillomas, adenomas, and carcinomas, may, in addition, to hematuria, cause *pain resembling colic*, due to the passage of a blood clot. These growths are revealed by the pyelogram and are treated by simple excision (benign polyp), nephrectomy, or ureterectomy or both.

Neoplasms of the bladder may be benign or malignant (Table XXX).

TABLE XXX

TISSUE	BENIGN	MALIGNANT
Epithelial	Papilloma	Carcinoma
	Leucoplakia	
Fibrous tissue	*Fibroma*	*Fibrosarcoma*
	Myxoma	Myxosarcoma
Nervous	Neurofibroma	Neurosarcoma
Blood vessels	Hemangioma	Angiosarcoma
Fat	Lipoma	Liposarcoma
Muscle	Leiomyoma	Leiomyosarcoma
	Rhabdomyoma	Rhabdomyosarcoma
Lymphoid		Lymphosarcoma, Hodgkin's disease, reticulum-cell sarcoma, plasmacytoma
Mixed	Dermoid	Malignant mixed tumor
		Embryoma

Fig. 427.—Primary carcinoma of the kidney. Note the extension of the growth into the renal pelvis.

From adjacent organs the more common extensions are from carcinoma of the rectum and cervix and endometriosis from the tubes, ovaries, or uterus. The most common of all primary tumors of the bladder are the epithelial types, papilloma and carcinoma. Although the cause of

carcinoma of the bladder is not known, there is a great incidence of the disease in men working with aniline dyes (Chapter 15). Men are affected six times more frequently than women. Early symptoms and signs are hematuria, urgency, frequency, and dysuria. Later, as the growths infiltrate, they involve the ureters and may break through the wall of the bladder to adjoining organs and tissues, spreading along nerve sheaths and finally involving lymphatics and blood vessels, causing metastases in the liver, lungs, lymph nodes, vertebrae, and other bones. Therefore,

Fig. 428.—Metastasis to the femur. A spontaneous fracture occurred. This is from the tumor shown in Fig. 427.

late symptoms are extremely variable, depending upon the degree of extension of the growth. Diagnosis is established early by examining the urine for cancer cells, cystoscopic examination, and biopsy. Intravenous pyelography is carried out to determine the possibility of ureteral occlusion or dilatation. Treatment depends upon the size and extensiveness of the growths. (1) Papillary tumors of small size are treated by endoscopic fulguration. (2) Papillary tumors of large size but with a narrow pedicle are treated by transurethral resection. (3) Papillary

tumors of large size with a broad base may be resected through a suprapubic cystotomy. (4) Massive involvement of the bladder requires ureteral transplantation and cystectomy. The transplanted ureters may be cutaneous or into the bowel. If the former is done because of great ureteral dilatation or obesity, one ureter may be tied and one transplanted, thereby avoiding two cutaneous openings. (5) Involvement from adjacent organs requires resection of the involved part along with the primary growth or total cystectomy may be done with abdomino-

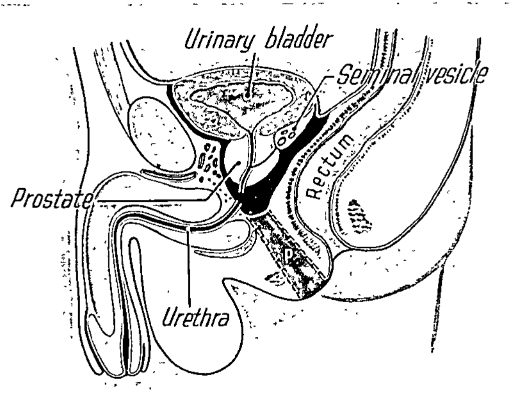

Fig. 429.—Diagram illustrating total cystectomy. This operation is indicated for carcinomas of the bladder or vesical neck or prostate and is done either by the abdominal route, when the lesion is far from the bladder neck, or by the combined perineal-abdominal route, when the carcinoma involves the bladder neck. We have employed the abdominal operation in practically all cases. The combined operation is done in two stages. The first stage consists of transplantation of the right ureter into the sigmoid colon or transplantation of both ureters at the same time. We have practiced the latter technique because by forming a flap of peritoneum and instituting stab wound drainage in both loins we do not fear leakage as we formerly did. Furthermore, the anastomosis between the ureter and the bowel is done by an oblique division of the ureter and mucosa-to-mucosa suture, then inversion of the sigmoid colon over the ureter, thereby protecting the peritoneal cavity from any leakage. Lastly, the lateral margin of the peritoneum is tacked down over the inverted ureter.

At the second stage the total cystectomy, prostatectomy, bilateral seminal vesiculec- tomy, and posterior urethrectomy are performed. The perineal part of the operation is done through an incision in the perineum, first dividing the urethra and then freeing the prostate and seminal vesicle as illustrated in the diagram (*P*). Then the abdominal part of the operation is done in which the bladder is extirpated in its entirety. If the lesion is far from the bladder neck, abdominal excision is preferable and bilateral trans- plantation and excision of the bladder may be done in one stage in patients who are in good condition. More recently the abdominal route alone has been used even in vesical neck carcinomas. The retropubic approach from above enables the surgeon to control the bleeding more completely and expeditiously, particularly that which ensues from the superior vesical and prostatico-vesical plexus. In carcinomas of the rectum which have invaded the bladder, the second stage consists of abdomino-perineal resection of the rectosigmoid along with the bladder as shown above.

perineal resection and bilateral transplantation *of the ureters.* (6) *Late cases* not suitable for operation may have ureteral transplantation and x-ray therapy *for palliation.* (7) Cases not suitable for surgery because of concomitant disease may be treated *by radon implants.*

Cystectomy may be performed in one, two, or three stages and may be done through the abdomen or by combined abdominoperineal resection. *Many prefer all in one stage.* This can be done if the ureters are transplanted into the skin. *A more desirable technique is the transplantation of both ureters into the sigmoid transperitoneally.* At this time exploration is done for metastases. If the lesion is far from the bladder neck, abdominal excision suffices. If the growth involves the bladder neck, abdominoperineal *resection* is required in which the bladder, seminal vesicles, prostate, and posterior urethra are removed en *masse. In males* the perineal portion of the operation is done first. The *urethra is tied and divided as far out as necessary; then the prostate and* bladder neck and seminal vesicles are mobilized, drains are introduced, and the suprapublic operation is done. Recently we have found that the entire operation may be done in one stage through the abdomen in good-risk patients. Even in carcinomas of the vesical neck, complete extirpation may be *accomplished by* the abdominal route with less *blood loss* and shock than with the *combined methods.*

A refinement of technique in the creation of an artificial bladder has been the use of isolated segments of bowel. These may be satisfactory when the *sigmoid colon* is used. However when the cecum is employed, even though it is used as an isolated pouch (with ureters implanted into the cecum and the distal end of the ileum brought to the outside), absorption of waste products may occur, producing azotemia and *uremia.*

Although *retention* or reabsorption of *nitrogenous waste* is associated with *uremia, there is no proof* that urea, uric acid, or creatinine is responsible for the symptoms. None of these is toxic in large doses, and experimental implantation of the ureters in the small intestine with reabsorption of urine and an increase of urea nitrogen to 800 or 900 mg. per cent may fail to produce symptoms of uremia. Yet the intravenous *injection of amino acid solution* aggravates *the symptoms.* Perhaps the symptoms *are due in part* to a reduction of ionized calcium in the body fluids (see Chapter 22) which may be the result of phosphate retention, and in addition the hyperchloremia which ordinarily occurs. We have recently made studies on patients with transplanted ureters, and we have found that the clinical picture of uremia *may* be present even though *blood* chlorides and ionized calcium *values are* within normal limits. There is, however, an elevation of urea nitrogen, uric acid, and creatinine in such cases. Because of the above, these patients are put on a restricted salt diet and 15 grains of sodium bicarbonate three times a day.

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